Research Article

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Evaluation of Exposure to HAV and Vaccination Status of Chronic HBV Cases - A Nationwide Multicenter Study

Kronik HBV Olgularında HAV Maruziyeti ve Aşılanma Durumunun Değerlendirilmesi - Ülke Çapında Çok Merkezli Bir Çalışma

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ABSTRACT

Objectives: Patients diagnosed with chronic hepatitis B virus (HBV) should be tested for hepatitis A virus (HAV) and vaccinated if they are seronegative. However, this test is often neglected. This study aims to investigate the status of HAV testing in chronic HBV patients.

ÖZ

Amaç: Kronik hepatit B virüs (HBV) tanısı alan hastaların hepatit A virüsü (HAV) açısından tetkik edilmesi ve seronegatif olanların aşılanması gereklidir. Ancak bu tetkik genellikle ihmal edilmektedir. Bu çalışmada kronik HBV hastalarına HAV açısından tetkik yapılma durumunun araştırılması amaçlanmıştır.

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Materials and Methods: A multicenter study is being conducted by the Viral Hepatitis Combat Association with 16 centers across the country, including patients who have been receiving treatment for chronic HBV for at least 14 years. The anti-HAV immunoglobulin G (IgG) testing and vaccination status of the patients in this study were evaluated retrospectively. The patients' data recorded in a web-based program were transferred to an Excel form, and the necessary analyses were performed. Statistical analysis was performed using SPSS for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Categorical measurements were summarized as numbers and percentages, continuous measurements as mean and standard deviation, and chi-square or Fisher's exact test statistics were used to compare categorical variables.

Results: The study group included 2966 individuals, 1832 of whom were male (61.8%) and 1134 of whom were female (38.2%). Of these patients, 1819 individuals (61.3%) were tested for anti-HAV IgG, while 1147 individuals (38.7%) were not. Of the 1819 individuals tested for anti-HAV IgG, 1688 (92.8%) were seropositive, and 131 (7.2%) were seronegative. It was determined that seropositivity increased significantly with age, and seronegativity was 23% among those aged 18-26 and 21% among those aged 27-33 (p=0.00001). According to the obtained data, HAV seronegativity was detected in one-fourth of individuals younger than 26 years and one-fifth of individuals aged 27-33. At 40 and above, seronegativity decreases significantly, falling to 5% and below.

Conclusion: Due to the changes observed in HAV epidemiology in our country in recent years, HAV seronegativity is high in young adults. According to our study data, anti-HAV IgG should be tested once in all chronic HBV patients, especially patients under the age of 35, and vaccination of seronegative individuals should not be neglected.

Keywords: Chronic HBV, HAV, vaccination, seroprevalence

Gereç ve Yöntemler: Viral Hepatitle Savaşım Derneği tarafından ülke genelinde toplam 16 merkezin katıldığı ve en az 14 yıldır kronik HBV tanısıyla tedavi görmekte olan hastaların dahil edildiği çok merkezli bir çalışma yürütülmektedir. Bu çalışmadaki hastalara anti-HAV immünoglobulin G (IgG) bakılma ve aşılanma durumları retrospektif olarak değerlendirilmiştir. Web tabanlı bir programa kaydedilen hastaların verileri Excel formuna aktarılarak gerekli analizler yapılmıştır. İstatistiksel analizler SPSS for Windows, sürüm 22.0 (IBM Corp., Armonk, NY, ABD) kullanılarak gerçekleştirildi. Kategorik ölçümler sayı ve yüzde olarak, sürekli ölçümlerde ortalama ve standart sapma olarak özetlenmiş, kategorik değişkenlerin karşılaştırılmasında ki-kare test ya da Fisher'ın kesin testi istatistiği kullanılmıştır.

Bulgular: Çalışma grubunda 1832'si erkek (%61,8), 1134'ü kadın (%38,2) olmak üzere toplam 2966 kişi yer almaktadır. Bu hastalardan 1819 kişiye (%61,3) anti-HAV IgG bakılmış, 1147 kişiye ise (%38,7) bakılmamıştır. Anti-HAV IgG bakılan 1819 kişiden 1688'i (%92,8) seropozitif, 131 kişi ise (%7,2) seronegatif olarak saptanmıştır. Yaşla birlikte seropozitifliğin belirgin şekilde arttığı ve 18-26 yaş arasında seronegatifliğin %23, 27-33 yaş arasında da %21 olduğu saptanmıştır (p=0,00001). Elde edilen verilere göre 26 yaştan genç bireylerin dörtte birinde, 27-33 yaş arası bireylerin de beşte birinde HAV seronegatifliği saptanmıştır. Kırk yaş ve üzerinde seronegatiflik anlamlı şekilde azalmakta, %5 ve altına inmektedir.

Sonuç: Ülkemizde son yıllarda HAV epidemiyolojisinde gözlenen değişim nedeniyle genç erişkinlerde HAV seronegatifliği yüksek saptanmaktadır. Çalışma verilerimize göre özellikle 35 yaş altındaki hastalar öncelikli olmak üzere tüm kronik HBV hastalarına bir kere anti-HAV IgG bakılması ve seronagatif bireylerin aşılanması ihmal edilmemelidir.

Anahtar Kelimeler: Kronik HBV, HAV, aşılama, seroprevalans

Introduction

Hepatitis A virus (HAV) infection continues to be the most common type of viral hepatitis in the world. The agent is an RNA virus in the *Hepatovirus* genus of the *Picornaviridae* family and is very resistant to environmental conditions and can survive for months under suitable conditions. The only natural host of the HAV is humans; it has six genotypes (I-VI) and a single serotype. When the disease is contracted, it is usually self-limiting in individuals with a healthy immune system, and only supportive treatment is often sufficient. Acute HAV infection does not become chronic, but acute liver failure can be seen in less than 1% of people over the age of 40 or those with underlying diseases (1,2,3,4,5,6).

Highly effective and reliable vaccines have been used to protect against HAV infection for years (2). In its 2022 update on the HAV vaccine (HAV position paper), the World Health Organization recommended that vaccination against the HAV should be included in national vaccination schedules for individuals ≥12 months of age if indicated based on the following conditions (7). These conditions include an increasing trend over time for acute HAV disease, including severe disease in older children, adolescents, or adults; a change in endemicity from high to moderate; and cost-effectiveness issues. This update also emphasizes that, with changing epidemiology, vaccination coverage may be expanded to adults in high-risk settings, the elderly, men who have sex with men, and other special populations such as homeless persons (6,7).

Materials and Methods

Method

A multicenter study is being conducted by the Viral Hepatitis Combat Association with 16 centers across the country, including patients who have been receiving treatment for chronic hepatitis B virus (HBV) for at least 14 years. The study plan includes patients who started treatment in 2010 and later and who received treatment for at least 12 months, and the data of the patients up to the end of 2024 were evaluated. The anti-HAV immunoglobulin G (IgG) testing and vaccination status of the patients in this study were evaluated retrospectively. The patients' data recorded in a web-based program were transferred to an Excel form, and the necessary analyses were performed.

Statistical Analysis

Statistical evaluation was performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Categorical measurements were summarized as numbers and percentages, continuous measurements as mean and standard deviation, and the chi-square test or Fisher' exact test statistics were used to compare categorical variables.

Our institution has received ethical approval from the Clinical Research Ethics Committee of İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine (approval number: A-83, date: 06.07.2021).

Results

The study group included 2966 people, 1832 of whom were male (61.8%) and 1134 of whom were female (38.2%). Of these patients, 1819 (61.3%) were tested for anti-HAV IgG, while 1147 (38.7%) were not. Of the 1819 people who were tested for anti-HAV IgG, 1688 (92.8%) were seropositive, and 131 (7.2%) were seronegative (Table 1). Of the 2966 patients included in the study, 1819 (61.3%) underwent serological screening for HAV, while 1147 (38.7%) were not. Of the 1819 patients screened for HAV, 1141 (62.7%) were male and 678 (37.3%) were female. Of the 1147 patients not screened, 691 (60.2%) were male and 456 (39.8%) were female. No statistically significant difference was found between genders in terms of HAV screening (p=0.17323).

It was determined that 32 of the 1688 people with known HAV results and seropositivity were immune to the vaccine, and 1656 were naturally infected and became immune.

When the distribution of anti-HAV IgG positivity was examined according to gender, 639 (23.7%) of 1688 HAV-positive individuals were female, and 1049 (62.2%) were male; 31 (23.7%) of 131 HAV-negative individuals were female, and 100 (76.3%) were male; the study group was predominantly composed of male patients.

There was no association between HAV testing in chronic HBV patients and gender (p=0.17323), and HAV IgG positivity was observed to be higher in both genders (p=0.001634) (Table 1).

When HAV positivity was evaluated according to age groups, it was determined that seropositivity increased significantly with age, and seronegativity was 23% between the ages of 18-26 and 21% between the ages of 27-33 (p=0.00001) (Table 2). According to the data obtained, HAV seronegativity was detected in one-fourth of individuals younger than 26 and one-fifth between the ages of 27-33. Seronegativity decreases significantly at age 40 and above, falling to 5% and below (Table 2).

When the relationship between HAV testing and the year of diagnosis was evaluated, the HAV testing rate was higher in those with an older year of diagnosis (Table 3).

When the relationship between HAV testing and the geographical region where the patients live was examined, it was determined that the highest rate of testing was done in people living in the Aegean region (82%), followed by the Marmara region (75%). The lowest testing rates were in the Eastern Anatolia (26.5%) and Southeastern Anatolia (26.5%) regions. It was also determined that the number of people vaccinated for HAV was higher in those living in the Aegean and Marmara regions (Figure 1).

Table 1. Anti-HAV IgG result by gender

Gender	HAV IgG pozitive	HAV IgG negative	Total
Male	1049 (91.3%)	100 (8.7%)	1149
Woman	639 (95.4%)	31 (4.6%)	670
Total	1688	131	1819

The row percentage was taken. *p=0.001634
HAV: Hepatitis A virus, IgG: Immunoglobulin G

Discussion

In recent years, it has been observed that there has been a significant change in the epidemiology of HAV in the world and in our country due to both infrastructure improvements and national vaccination programs. In a review examining the trends reported in the literature between 2000 and 2021 in the epidemiology of HAV in the Western Pacific Region, it was reported that many countries moved from high endemicity to low endemicity, the administration of HAV vaccination in children shifted the susceptibility to the disease to the elderly population, and while seroprevalence among children decreased in most countries, almost 100% seropositivity was observed in middle adulthood (8).

To determine the current epidemiological characteristics of HAV in European countries, a systematic literature review was conducted on articles published on HAV in 11 European countries (Denmark, France, Germany, Greece, Hungary, Italy, the Netherlands, Spain, Sweden, Switzerland and the United Kingdom) in the last twenty years, and PubMed and Embase data were used between January 1, 2001 and April 14, 2021. According to this assessment, acute HAV cases have decreased in Europe since 1990. Still, there are differences from country to country, and routine vaccination also varies from country to country (9).

Table 2. Anti-HAV IgG positivity by age groups

Age groups	Ages	Anti-HAV IgG positive	Anti-HAV IgG negative	Total
After 2000	24	10 (77%)	3 (23%)	13
1999-1998	25-26	10 (77%)	3 (23%)	13
1997-1991	27-33	124 (79.5%)	32 (20.5%)	156
1990-1985	34-39	190 (84%)	36 (16%)	226
1984-1974	40-50	508 (94.6%)	29 (5.4%)	537
1973-1963	51-61	517 (96.8%)	17 (3.2%)	534
1962-1952	62-72	260 (9.6%)	10 (3.4%)	270
1951-1941	73-83	61 (98.4%)	1 (1.6%)	62
1940+	84+	8 (100%)	0	8
Total		1688 (92.7%)	131 (7.2%)	1819

*Percentage of rows, p=0.001
HAV: Hepatitis A virus, IgG: Immunoglobulin G

Table 3. The relationship between the year of diagnosis and anti-HAV IgG detection of chronic HBV patients

Year of diagnosis	HAV screening (+)	HAV screening (-)	Total
2020 and beyond	96 (62%)	61 (38%)	157
2019-2015	554 (56%)	436 (44%)	990
2014-2010	808 (67%)	400 (33%)	1212
2009-2001	271 (61%)	172 (39%)	443
2000 and earlier	82 (77%)	24 (23%)	106

*p<0.001
HAV: Hepatitis A virus, IgG: Immunoglobulin G, HBV: Hepatitis B virus

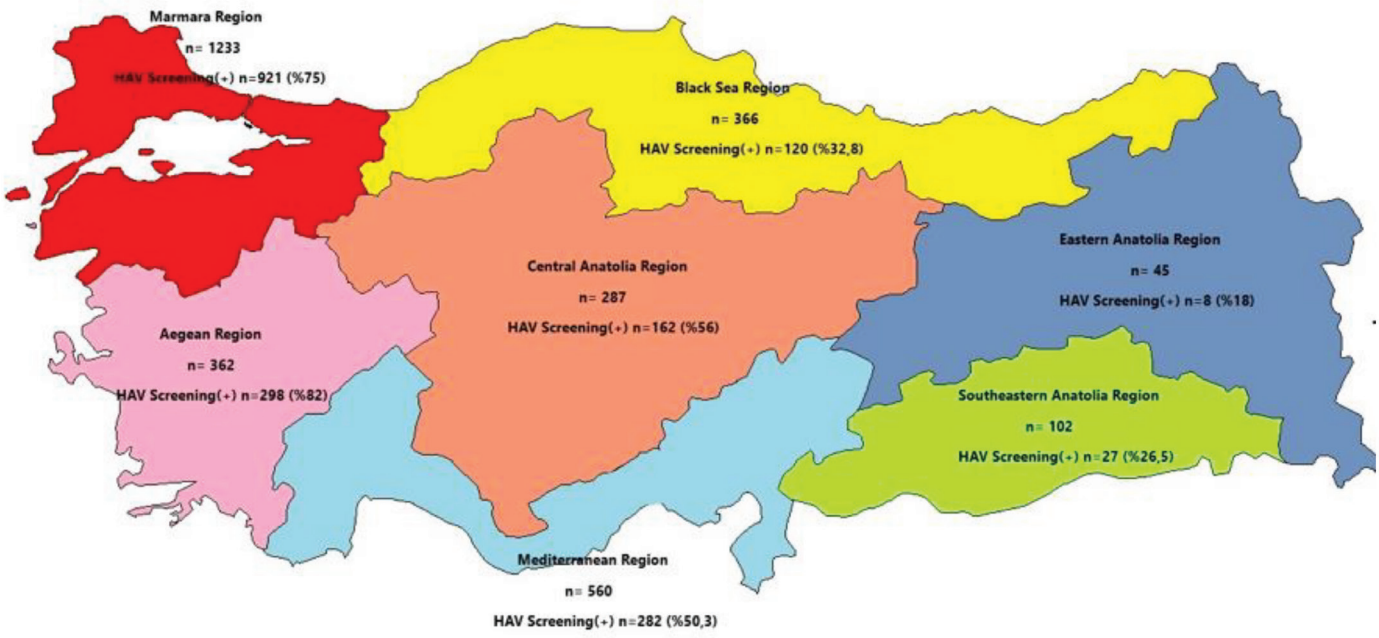

Figure 1. The relationship between HAV examination and the geographical region (n=2955)
HAV: Hepatitis A virus

A recent review, including our country's data, examined publications on HAV epidemiology before and after implementing the childhood HAV vaccination program in Türkiye and reported a significant change in the age of first HAV exposure (10). A meta-analysis recently published in our country scanned studies on HAV published between January 1, 2000, and December 31, 2023, that met the inclusion criteria. Data were obtained from all geographical regions of Türkiye, and the overall prevalence of HAV in the population was 53% (11). Another systematic meta-analysis conducted to evaluate age-specific HAV seroprevalence rates in Türkiye between 2000 and 2023 included 57 articles. HAV seroprevalence was found to be 90.90% in the >35 age group, and the overall seroprevalence estimated using a random effects model was reported as 64.5% (12).

It is known that acute HAV infection progresses more severely in individuals with immunosuppressive conditions or chronic liver disease and that the prognosis is worse when acute hepatitis is added to chronic hepatitis, especially in the presence of damaged livers (7,13).

In a study examining HAV outbreaks seen in the last 20 years in the European region, deaths were reported from five countries (Spain, Denmark, Germany, Hungary, and Italy) during the outbreaks seen in the last 20 years. The case fatality rate was determined to be between 0.05% and 0.26% (14). This analysis also examined the underlying conditions in the fatal cases. These conditions were defined as preexisting liver diseases (such as HBV or HBC infection), HIV infection, renal failure, diabetes, intravenous drug use, pulmonary neoplasia, and pulmonary edema; 70% of the deceased were reported to be ≥60 years of age.

In the United States of America, 33 outbreaks and 37,553 acute HAV cases were seen between 2016 and 2020; 56% of the cases that could be reached were drug addicts, 14% were homeless, 61% of the cases were hospitalized, and 380 people died (15). When the histories of the deceased were examined, it was determined that they had past or current HBV (5%) or HCV (30%) infection. In the large HAV outbreak in Shanghai, China, in 1988, 310,746 cases were seen, and a total of 47 deaths (0.015%) occurred (16). Mortality rates were 0.05% (15/27.346) vs 0.009% (25/283.400) in patients with and without HBV infection, respectively, with a 5.6-fold higher mortality rate in patients with chronic HBV infection than in those without. In this study, Cooksley (16) reported that HBV-infected patients with elevated alanine aminotransferase levels and elevated HBV-DNA levels were at higher risk of liver failure following HAV superinfection. As seen in many similar studies, acute HAV infection in individuals with underlying chronic liver disease can progress severely and even lead to death.

International guidelines also include vaccination of seronegative chronic HBV and HCV patients (17). In our country, vaccination of seronegative individuals in the risk group (including chronic HBV and HCV patients) has been provided free of charge by the Ministry of Health for many years. In addition, the national HAV vaccination was started in October 2012 to be applied to babies aged 18-24 months, and all babies born in March 2011 and later are vaccinated. In connection with this, a very significant decrease in acute HAV infection is observed, especially in children and adolescents (18). Chronic HBV and HCV patients are always included as a risk group regarding HAV vaccination in the hepatitis prevention programs of the Ministry of Health (19). However, many studies conducted worldwide have shown that the HAV screening and vaccination rates of patients with chronic liver disease are not at the desired level. A gastroenterology clinic in the United States of America determined that 50% of 141 chronic liver disease patients with an average age of 54 who were followed up between 2014 and 2015 were vaccinated against HAV, and 46% were vaccinated against

HBV (20). In Iran, when blood was taken from a total of 403 chronic HBV patients between 2016 and 2017 and anti-HAV IgG was tested, it was reported that 379 (94%) were seropositive. None of them had been vaccinated against HAV (21). The average age of the participants in this study was 29 in seronegative individuals and 42 in seropositive individuals. Since the age groups with the highest HAV seronegativity are under 25 and between 25-35 years, it was commented that it would be appropriate to test for HAV in patients younger than 35 years. In a study conducted in Korea between 2008-2010, anti-HAV IgG results were evaluated in chronic HBV and HCV patients and healthy community members, and it was determined that the seroprevalence was similar to the general population (52.5% in the community, 49% in chronic hepatitis patients). In this study, seronegativity was high in those aged 35 and under. Therefore, it was recommended that chronic hepatitis patients in these age groups be tested and vaccinated (22). In another study from Korea, the prevalence of HAV IgG was determined as 86.6% in 986 patients, 714 of whom were male, over 40 years of age (average age 50) with chronic liver disease between 2008-2009 (80% in chronic HBV, 87% in chronic HCV; 93.8% in HBV-related cirrhosis, 100% in HCV-related cirrhosis). As a result, it was reported that most people over 40 years of age had encountered HAV; the distribution by age groups was as follows: in their 20's (6.67%), in their 30's (50.86%), in their 40's (92.29%), in their 50's (97.77%), and over 60's (100%) (23). In Konya, a province located in a medium-high endemic region in terms of HAV seropositivity in our country, HAV seropositivity was examined in chronic HBV and HCV patients between 2011-2014 and was found to be 97.5% in chronic HBV patients and 93.6% in chronic HCV patients (average 94%). Independent risk factors were determined as being younger than 40 and living in a rural area (24). In another study conducted in our country between 2009-2013, a total of 673 chronic HBV patients, 354 male and 319 female, aged between 17-78, were included, and HAV IgG positivity was found to be 34% in those younger than 20 years of age, 79% in those aged between 20-29 years, and 100% in those aged 35 and over (25).

Our study determined that 1819 (61.3%) out of 2966 patients were tested for anti-HAV IgG, and 1147 (38.7%) were not. Our results are similar to other studies in our country, and the rate of chronic HBV in which HAV was not tested is as high as 40%. In our study, 1688 (92.8%) out of 1819 patients tested for anti-HAV IgG were seropositive, and 131 (7.2%) were seronegative. However, since almost half of the patients were not tested for HAV, it was impossible to learn the HAV exposure/vaccination status of these patients. However, according to the available data, one in four patients younger than 27 years of age (born in 1998 and after) were seronegative for HAV. This rate drops to one in five in the 27-33 age group (born between 1997-1991) and 16% in the 34-39 age group (born between 1990-1985). HAV seronegativity decreases significantly in those born at or above 40 (1984 and before), falling below 5%. According to these results, the probability of detecting HAV seronegativity is high in chronic HBV patients under the age of 40 and especially under the age of 30; therefore, testing should not be neglected, especially in these age groups. Although HAV seropositivity increases with age, it is striking that there are seronegative patients even at older ages, although their numbers are very low. Therefore, the idea is to test all chronic HBV patients for anti-HAV IgG once in their lifetime. Since our country was a medium-high endemic region in terms of HAV epidemiology in the past years, the general approach of physicians was that adults had already contracted HAV infection naturally, and therefore, there was no need for testing. However, this change in HAV epidemiology should not be ignored today.

When the relationship between anti-HAV IgG testing and the year of diagnosis was evaluated as expected, the HAV testing rate was higher in those with an older year of diagnosis. This result was thought to be related to the fact that patients had visited different hospitals/physicians over the years, and the possibility of having anti-HAV IgG tested at any time increased.

When the relationship between anti-HAV IgG testing and the geographical region where the patients lived was examined, it was determined that the highest rate of testing was done in patients living in the Aegean region (82%), followed by patients residing in the Marmara region (75%) (Figure 1). The lowest rates were in the Eastern Anatolia (26.5%) and Southeastern Anatolia (26.5%) regions. This may be because the majority of patients are numerically higher in these regions, and physicians in these regions show more interest in the subject. It has been determined that the number of people vaccinated for HAV is higher in those living in the Aegean and Marmara regions.

When the relationship between the anti-HAV IgG test and the geographical region where the patients were born is examined, the highest test rates were found in those born in the Aegean (79%), abroad (77%), Marmara (73%), Central Anatolia (68%), Eastern Anatolia (64%), Southeastern Anatolia (58%), Mediterranean (51%) and Black Sea (49%) regions, respectively.

A pleasing situation observed in the study data is that the majority of chronic HBV patients in the study group were born in 1997 and above (25-27 years of age and above), and the highest number of patients were in the 34-39 age group (birth years between 27-50 years of age). Chronic HBV patients born after the national vaccination program started in 1998 constituted only 1.4% (26/1819) of the study group. This situation is thought to be closely related to the national HBV vaccination program started in our country in 1998; thus, it was observed that the rate of chronic HBV in individuals born after the vaccination program decreased statistically significantly ($p<0.00001$) (Table 3).

Study Limitations

The study's limitation is that some data were difficult to access due to the retrospective collection of data. However, it is thought that the data may reflect the approaches of physicians who follow chronic HBV patients throughout the country, and it is anticipated that these data may create awareness among physicians who follow chronic HBV cases.

Conclusion

As a result, the number of chronic HBV cases among young people is gradually decreasing as a result of national vaccination programs in our country, and there is also a positive change in HAV epidemiology. Since childhood HAV vaccination has been started in our country since 2011, we are likely to encounter HAV seronegative individuals for approximately one more decade.

Considering the severe course of acute HAV infection in individuals with chronic hepatitis, all chronic HBV patients, regardless of their age, should be tested for HAV once, and seronegative individuals should not be neglected to be vaccinated.

Ethics

Ethics Committee Approval: Our institution has received ethical approval from the Clinical Research Ethics Committee of İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine (approval number: A-83, date: 06.07.2021).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: S.T., F.T., R.G., Design: S.T., F.T., R.G., Data Collection or Processing: S.T., A.B., E.Y.Z., M.A., E.T., E.P., M.O.T., T.T., D.Y.S., Y.Ö., U.B., İ.E.Y., O.K., A.Ö., H.D.Ö., F.T., M.N.T., S.A., B.K., S.K., A.S.Ö., L.N.A., R.G., Analysis or Interpretation: S.T., F.T., R.G., Literature Search: S.T., Writing: S.T.

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References

1. Wang M, Feng Z. Mechanisms of hepatocellular injury in hepatitis A. Viruses. 2021;13:861.
2. Nelson NP, Weng MK, Hofmeister MG, Moore KL, Doshani M, Kamili S, Koneru A, Haber P, Hagan L, Romero JR, Schillie S, Harris AM. Prevention of hepatitis A virus infection in the United States: recommendations of the advisory committee on immunization practices, 2020. MMWR Recomm Rep. 2020;69:1-38.
3. Devarbhavi H, Asrani SK, Arab JP, Nartey YA, Pose E, Kamath PS. Global burden of liver disease: 2023 update. J Hepatol. 2023;79:516-537.
4. Girish V, Grant LM, John S. Hepatitis A. 2024 Oct 6. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
5. Mehta P, Grant LM, Reddivari AKR. Viral hepatitis. [Updated 2024 Mar 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554549/
6. Van Damme P, Pintó RM, Feng Z, Cui F, Gentile A, Shouval D. Hepatitis A virus infection. Nat Rev Dis Primers. 2023;9:51.
7. World Health Organization. WHO position paper on hepatitis A vaccines. Wkly Epidemiol Rec. 2022;97:493-512. Available from: https://www.who.int/teams/immunization-vaccines-and-biologicals/policies/position-papers/hepatitis-a (accessed 2025 Jan 26).
8. Gloriani NG, de Paz-Silava SLM, Allison RD, Takashima Y, Avagyan T. The shifting epidemiology of hepatitis A in the World Health Organization Western Pacific region. Vaccines (Basel). 2024;12:204.
9. Andani A, Mellou K, Dewda P, Eeuwijk J, Kassianos G, Van Damme P, Steffen R. Evolution and impact of hepatitis A epidemiology in Europe-systematic literature review of the last 20 years. J Viral Hepat. 2025;32:e14030.
10. Badur S, Öztürk S, Ozakay A, Khalaf M, Saha D, Van Damme P. A review of the experience of childhood hepatitis A vaccination in Saudi Arabia and Turkey: implications for hepatitis A control and prevention in the Middle East and North African region. Hum Vaccin Immunother. 2021;17:3710-3728.
11. Karakaya Suzan Ö, Bektaş M, Altındiş M, Kaya Ö, Eroğlu A, Çetinkaya Özdemir S, Tecik S, Emecen AN, Çınar N. Examining the changes in the prevalence of Hepatitis a in Türkiye: systematic review and metaanalysis. BMC Public Health. 2024;24:3280.
12. Ciftci IH, Koroglu M, Demiray T, Terzi HA, Kahraman Kilbas EP. Age-specific seroprevalence of hepatitis A virus in Turkey between 2000 and 2023: systematic review and meta-analysis. Diagnostics (Basel). 2024;14:2464.
13. Kanda T, Sasaki R, Masuzaki R, Takahashi H, Mizutani T, Matsumoto N, Nirei K, Moriyama M. Co-occurrence of hepatitis A infection and chronic liver disease. Int J Mol Sci. 2020;21:6384.
14. Andani A, Bunge E, Kassianos G, Eeuwijk J, Mellou K, Van Damme P, Mukherjee P, Steffen R. Hepatitis A occurrence and outbreaks in Europe over the past two decades: a systematic review. J Viral Hepat. 2023;30:497-511.
15. Foster MA, Hofmeister MG, Yin S, Montgomery MP, Weng MK, Eckert M, Nelson NP, Mermin J, Wester C, Teshale EH, Gupta N, Cooley LA; Hepatitis A Response Team. Widespread hepatitis A outbreaks associated with person-to-person transmission - United States, 2016-2020. MMWR Morb Mortal Wkly Rep. 2022;71:1229-1234.
16. Cooksley WG. What did we learn from the Shanghai hepatitis A epidemic? J Viral Hepat. 2000;7 (Suppl 1):1-3.
17. Terrault NA, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, Brown RS Jr, Bzowej NH, Wong JB. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Clin Liver Dis (Hoboken). 2018;12:33-34.
18. Kanik-Yüksek S, Tezer H, Parlakay AÖ, Gülhan B, Kara A, Çiftçi E, Tapısız A, Çelik M, Özdemir H, Aykaç K, Demirdağ TB, Kara TT, Hayran G, İnce E. Impact of the mandatory hepatitis A immunization program: before and after the vaccine in Ankara, central of Turkey. Turk J Pediatr. 2019;61:677-685.
19. Ministry of Health. Turkish viral hepatitis prevention and control program (2018–2023). 1st ed. Ankara: Ministry of Health; 2018. Available from: https://hsgm.saglik.gov.tr/depo/birimler/bulasici-hastaliklar-ve-erken-uyari-db/Dokumanlar/Rehberler/TVHOKP-Eng.pdf [accessed 2025 Feb 2].
20. Tajammal R, Ali IA, Syed T, Nusrat S. Immunization against hepatitis A virus and hepatitis B virus in patients with chronic liver disease: are we doing a good job? Cureus. 2018;10:e2528.
21. Manshadi SAD, Alijani N, Salehi M, Dadras O, SeyedAlinaghi S, Ahangari A, Abdolahi A, Davoudi H, Alizade R. Hepatitis A seroprevalence among patients with chronic hepatitis B infection: a cross-sectional study in Iran during 2016-2017. Infect Disord Drug Targets. 2020;20:748-751.
22. Lee SH, Kim HS, Park KO, Park JW, Chun SY, Lim SJ, Cho HJ, Kim SJ, Park HW, Moon HK, Shin WG, Kim KH, Jang MK, Lee JH, Kim HY. Prevalence of IgG anti-HAV in patients with chronic hepatitis B and in the general healthy population in Korea. Korean J Hepatol. 2010;16:362-368.
23. Cho HC, Paik SW, Kim YJ, Choi MS, Lee JH, Koh KC, Yoo BC, Son HJ, Kim SW. Seroprevalence of anti-HAV among patients with chronic viral liver disease. World J Gastroenterol. 2011;17:236-241.
24. Özden HT. Hepatitis A seroprevalence in patients with chronic viral hepatitis in Konya, Turkey. Eur J Gastroenterol Hepatol. 2016;28:333-337.
25. Tulek N, Ozsoy M, Moroglu C, Cagla Sonmezer M, Temocin F, Tuncer Ertem G, Sebnem Erdinc F. Seroprevalence of hepatitis A virus antibodies among the patients with chronic hepatitis B in Turkey. Euroasian J Hepatogastroenterol. 2015;5:95-97.