



Ten Year Hepatitis A, B, And C Seroprevalence Trend in Children: Results From A Single Center

Çocuklarda On Yıllık Hepatit A, B ve C Seroprevalans Trendi: Tek Merkez Sonuçları

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Abstract

Aim: Hepatitis B vaccination since 1998 and hepatitis A vaccination since 2012 is available in the childhood routine vaccination program in Turkey. There is no vaccine for hepatitis C yet. The seroprevalence of hepatitis A, B, and C differs between regions. For this reason, each region should assemble its own rates. Therefore, this study aimed to determine the seroprevalence of hepatitis A, B, and C in children in Kastamonu province, to evaluate whether there is a change in prevalence according to years and patient age, and to review whether there is a change in hepatitis A virus seroprevalence with hepatitis A vaccination.

Material and Methods: File records of all patients under 18 whose hepatitis serology was studied at Kastamonu Training and Research Hospital between 01.01.2012 and 21.12.2021 were reviewed retrospectively.

Results: A total of 19885 patients and 55738 test results were included in the study. Accordingly, hepatitis A seroprevalence increased year by year. Anti-HAV IgG positivity was higher in the vaccinated group, whereas anti-HAV IgM positivity was higher in the unvaccinated group ($p<0.01$). Anti-HBs gradually decreased until the age of 13 and increased again thereafter. Anti-HCV was positive in 11 patients (0.1%).

Conclusions: Our study shows successful results of hepatitis A and hepatitis B vaccination. Therefore, we recommend that the extended immunization program carried out in Turkey be continued meticulously, and prevention methods should always be applied for hepatitis C.

Keywords: Hepatitis A, hepatitis B, hepatitis C, seroprevalence, children

Öz

Amaç: Türkiye’de çocukluk çağı rutin aşılama programında 1998’den beri Hepatit B aşısı, 2012’den beri hepatit A aşısı bulunmaktadır. Hepatit C için henüz bir aşı yoktur. Hepatit A, B ve C seroprevalansı bölgeler arasında farklılık gösterir. Bu sebeple her bölgenin kendi oranlarını göstermesi önemlidir. Bu çalışmada Kastamonu ilindeki çocuklarda hepatit A, B ve C seroprevalansının belirlenmesi, yıllara ve hasta yaşına göre prevalansında değişiklik olup olmadığının değerlendirilmesi ve hepatit A aşısı ile hepatit A virüsü seroprevalansında değişiklik olup olmadığının gözden geçirilmesi amaçlanmıştır.

Materyal ve Metod: Kastamonu Eğitim ve Araştırma Hastanesi’nde 01.01.2012-21.12.2021 tarihleri arasında hepatit serolojisi çalışılan 18 yaş altı tüm hastaların dosya kayıtları geriye dönük olarak incelendi.

Bulgular: Çalışmaya toplam 19885 hasta ve 55738 test sonucu dahil edildi. Buna göre hepatit A seroprevalansı yıldan yıla artış göstermiştir. Anti-HAV IgG pozitifliği aşı grubta daha yüksek iken, anti-HAV IgM pozitifliği aşısız grupta daha yüksekti ($p<0.01$). Anti-HBs değerinin 13 yaşına kadar giderek azaldığı, 13 yaşından sonra tekrar artış gösterdiği görüldü. Anti-HCV 11 hastada (%0.1) pozitif.

Sonuç: Hepatit A ve hepatit B aşılamasının başarılı sonuçları çalışmamızda fark edilmektedir. Ülkemizde yürütülen genişletilmiş bağışıklama programına titizlik ile devam edilmesini, hepatit C için de korunma yöntemlerine her zaman uyulmasını önermekteyiz.

Anahtar Kelimeler: Hepatit A, hepatit B, hepatit C, seroprevalans, çocuk

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INTRODUCTION

Hepatitis A virus (HAV) is a common cause of acute viral hepatitis in childhood. It is transmitted by the fecal-oral route. Although it does not become chronic, its most feared complication is acute liver failure. The severity of the acute infection increases with the patient's age. Although 1.5 million new cases worldwide are still seen annually, developing countries are at higher risk (1,2). For HAV seroprevalence, Turkey is in the moderate endemic group (3). Therefore, vaccination is essential for prevention. At the end of 2012, the HAV vaccine was included in Turkey's routine childhood vaccination calendar (4).

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are significant public health problems that can cause acute and chronic liver damage, and their clinical spectrum can range from asymptomatic infection to cirrhosis and hepatocellular carcinoma (5). Turkey is a low moderate area for HBV seroprevalence and a low endemic area for HCV seroprevalence (6-7). Hepatitis B vaccination has been in Turkey's routine childhood vaccination calendar since 1998. Unfortunately, there is no current vaccine for hepatitis C. According to the World Health Organization data, HBV and HCV caused 3 million new infections and 1.1 million deaths in 2019 (8).

In Turkey, the seroprevalence of HAV, HBV, and HCV differs between regions. For this reason, each region must monitor its own rates.

This study aimed to determine the seroprevalence of hepatitis A, B, and C in children in Kastamonu province, to assess whether there is a change in seroprevalence according to years and patient age, and to review whether there is a change in HAV seroprevalence with hepatitis A vaccination.

MATERIAL AND METHOD

The file records of all patients under 18 years old, whose hepatitis serologies were studied for any reason between 01.01.2012 and 21.12.2021 in the pediatrics and pediatric

surgery outpatient clinics of Kastamonu Training and Research Hospital were retrospectively scanned. The study was not designed as a community-based screening, records of patients admitted to our hospital were used. Anti-HAV IgM, anti-HAV IgG, anti-HBs, HBsAg, and anti-HCV values were determined using the Enzyme-Linked Immunosorbent Assay (ELISA) method according to the procedure prescribed by the manufacturer (Abbott Architect, USA). For the anti-HBs level, more than 10 mIU/liter was considered positive. File records were examined for HAV, patients who were born after March 2011 and were over 24 months old at the time of blood test were considered to be fully vaccinated for HAV. The study group was determined by removing multiple test entries for one person. The study group was determined by accepting only the most recent results if there was multiple test entries for one person. Approval of the study, dated 09.03.2022 and numbered 2022-KAEK-31, was obtained from the Ethics Committee of Kastamonu University Faculty of Medicine.

Data were analyzed in the SPSS 22.0 program. Descriptive statistics were given as numbers, percentages, and ratios. The sample of the study was formed as all patients whose data were accessed using the purposeful sampling method, and the normality of the distributions was determined using the Kolmogorov Smirnov test over the package program. The Chi-square test was used to compare non-parametric variables, and Student's t-test was used to compare parametric variables. In all statistical evaluations, $p < 0.05$ was accepted as significant.

RESULTS

A total of 19885 patients and 55738 test results were included in the study. Of the patients, 61.5% were male, and 38.5% were female. The mean age of the participants was 10.0 ± 5.0 (1-17 years). The distribution of tests was 1962 anti-HAV IgM, 1746 anti-HAV IgG, 14365 anti-HBs, 19434 HBsAg, and 18231 anti-HCV. The distribution of positivity and negativity of the tests is given in Table 1.

	Anti-HBs		HBsAg		Anti-HAV IgG		Anti-HAV IgM		Anti-HCV	
	n	%	n	%	n	%	n	%	n	%
Negative	4671	32.5	19401	99.8	1234	70.7	1865	95.1	18220	99.9
Positive	9694	67.5	33	0.2	512	29.3	97	4.9	11	0.1
Total	14365	100.0	19434	100.0	1746	100.0	1962	100.0	18231	100.0

	Anti-HAV IgG			p	Anti-HAV IgM			p
	Negative	Positive	Total		Negative	Positive	Total	
Unvaccinated	1225 (77.4%)	356 (22.6%)	1581	<0.01	1673 (94.5%)	97 (5.5%)	1770	<0.01
Vaccinated	2 (1.2%)	163 (98.8%)	165		192 (100%)	0 (0%)	192	
Total	1233	513	1746		1865	97	1962	

Chi Square test; $p < 0.05$

Distribution by years and age groups are given in Figure 1 and 2. Accordingly, hepatitis A seroprevalence increased yearly, and the rate of anti-HBs positivity decreased gradually until the age of 13 and increased after 13. Anti-HCV results of 18231 patients aged 0-18 years were evaluated, and it was positive in 11 (0.1%) children.

Anti-HAV IgG positivity was higher in the vaccinated group, and Anti-HAV IgM positivity was higher in the unvaccinated group ($p < 0.05$) (Table 2).

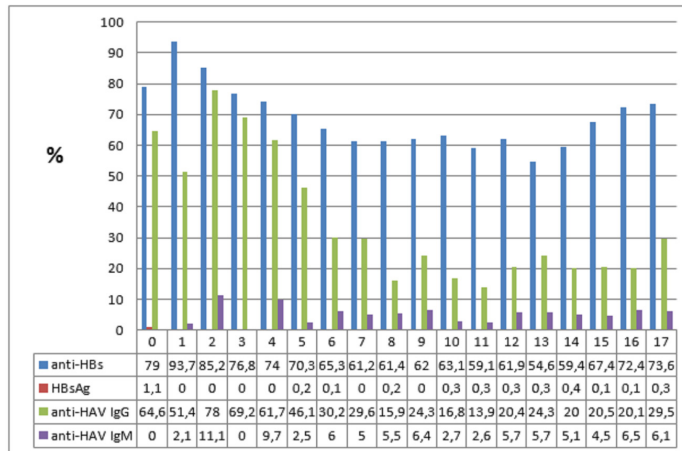


Figure 1. Distribution of anti-HAV IgM, anti-HAV IgG and anti-HBs, HBsAg seropositivity rates by patient age (years)

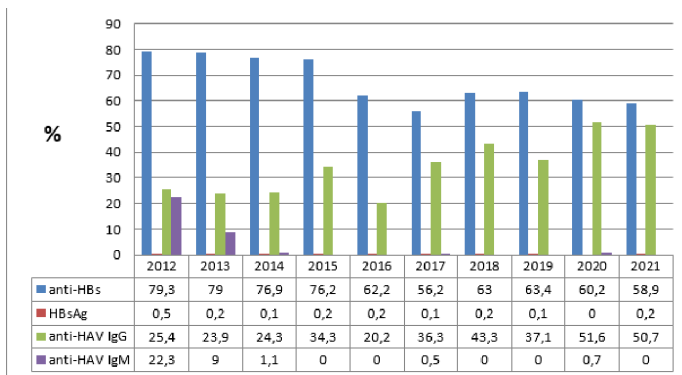


Figure 2. Distribution of anti-HAV IgM, anti-HAV IgG, anti-HBs and HBsAg seropositivity rates by years

DISCUSSION

Our study is the first to evaluate hepatitis A, B, and C seroprevalences in children in the Kastamonu province. Hepatitis A seroprevalence (percentage of anti-HAV IgG seropositivity) was 29.3% in children aged 0-17. The effect of hepatitis A vaccination, which was included in Turkey's extended immunization program at the end of 2012, was seen in our study. In our study, HAV seroprevalence was 25.4% in 2012, and 50.7% in 2021. In addition, it was observed that anti-HAV IgG seropositivity was significantly higher and anti-HAV IgM positivity was lower in HAV vaccinated children ($p < 0.01$). Anti-HBs positivity was 67%, HBsAg positivity was 0.2%, and anti-HCV positivity was 0.1%, and similar rates were found compared to other studies conducted in Turkey (2,9,10).

A seropositive result of anti-HAV IgG is accepted as an indicator of vaccine-acquired immunity or previous hepatitis A infection and creates permanent immunity to HAV (11,12). In a study conducted with 555 patients in Antalya province in 2022, hepatitis A seroprevalence was 24.7% in children aged 1-15 (13). In another study conducted in Karabük by Doğan et al., in 2017 with 200 patients, HAV seroprevalence was 28% (2). Our seroprevalence percentage is similar to these studies. Tekkanat et al., found that hepatitis A seroprevalence in children aged 0-18 in the Kars province in 2015 was 66.5%, while Okur et al., reported the rate as 69.9% in children in Van province in 2011, and Aslan et al., found the prevalence as 66.5% in children in Şanlıurfa in 2001 (14-16). Our seroprevalence being lower than these studies can be associated with our province's high level of socio-economic development and attention to hygiene conditions.

The Hepatitis A vaccine was included in Turkey's mandatory national immunization program in November 2012, the first dose being at the end of the 18th month, and the second dose at the end of the 24th month (4). The expected seroconversion after the first dose is 90%, and this rate reaches 100% after the second dose (17). In our study, we divided the patients we examined for anti-HAV IgG into two groups regarding whether they were vaccinated against hepatitis A. Anti-HAV IgG was positive in 22.6% in the unvaccinated group, while this rate was 98.8% in the vaccinated group. This significant difference reveals the success of the hepatitis A vaccine. In addition, when we evaluated anti-HAV IgG positivity according to age, it was seen that the highest prevalence was at the age of two (24-36 months). This peak can also be attributed to the age group being the first with complete vaccination. Not many studies in the literature evaluate the effect of hepatitis A vaccination on HAV prevalence in children in Turkey. In the study conducted by Kılıçaslan et al., with 762 pediatric patients, seroconversion was 88.4% in the vaccinated group and 34.9% in the unvaccinated group (18). We think that the increase in anti-HAV IgG seropositivity in the presence of a successful vaccination program will be demonstrated by future studies conducted in Turkey.

Anti-HBs and HBsAg are frequently used in screening for hepatitis B infections (19). In clinical practice, HBsAg positivity is the first step in diagnosing HBV-infected individuals (20). The first marker in the serum is HBsAg, which essentially indicates ongoing HBV infection. The serological marker of recovery is anti-HBs, which shows the immunity that develops after an infection or vaccination (17, 21). Therefore, it is essential to detect the patients infected with HBV in the screenings and to identify and vaccinate those who are negative by checking the anti-HBs levels of unvaccinated individuals. In Turkey, hepatitis B vaccination was included in the routine childhood vaccination chart in 1998. Newborns receive three doses, one right after being born, one in the 1st month and one in the 6th month. An anti-HBs level above 10 mIU/liter is considered positive and is an indicator of immunity (22). In the study by Kılıçaslan et al., with 192 patients aged 10-19 years old, anti-HBs

positivity rate was 61.9% (23). In another study by Duran et al., with 208 patients, this rate was 68.3% (9). Similarly, in the study of Sarigül et al., with 1546 pediatric patients, anti-HBs positivity was 69.9% (10). In our study, this rate was 67.5%, similar to the studies conducted in Turkey.

Another striking point in our study was that the age group with the highest anti-HBs positivity (93.7%) was toddlers (between 12-24 months). This rate decreased gradually towards the age of 13 and increased between 13-17. The reason for this change is the decrease in the protective titer value in the years after vaccination. Accordingly, risk factors can be counted as male gender, smoking, presence of obesity, as well as transferring the vaccine without complying with the cold chain, non-compliance with the vaccine schedule, and failure to apply the vaccine in an appropriate technique (23). The highest percentage of anti-HBs positivity being in the first age group of children whose vaccination program was completed as of the sixth month may be associated with the fact that they are the first age group after a completed vaccination. The percentage of anti-HBs, which was 54.6% at the age of thirteen, increased every year after this and was 73.6% at age 17. We think that the booster vaccination of individuals with low immune response in high school age played a role in the percentage of anti-HBs positivity rising in adolescence. We suggest that this change should be investigated with new studies.

HBsAg seroprevalence in children varies between regions. Studies have shown that HBsAg seroprevalence decreased with hepatitis B vaccination. In the study by Kösecik et al., on children in Şanlıurfa in 1997, HBsAg seroprevalence was 12.5% (24). This study is very valuable because it was done before the hepatitis B vaccine was included in childhood routine practice. In a study by Zeyrek et al., in Şanlıurfa in 2002, HBsAg seroprevalence was 2%, and the effects of the vaccine were observed (25). HBsAg seroprevalence was 0.2% in the study of Kaya et al., in children in the Van region in 2010, 0.2% in the study of Doğan et al., in children in Karabük in 2017, and 0.08% in the study of Altan et al., in children in 2017 (2,26,27). In our study, HBsAg seroprevalence was 0.2%, similar to the studies conducted in the pediatric age group in recent years.

HCV is the most common cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma in adults in developed countries. About 170 million people worldwide are infected with HCV, and almost 3 million new individuals join this group each year. The prevalence under the age of twenty is lower. It is transmitted by the percutaneous or parenteral transmission of infected blood, blood products, or body fluids. Vertical (perinatal) transmission has recently been at the forefront in children. The first test to be used within the scope of HCV infection screening is anti-HCV. In case of anti-HCV positivity or anti-HCV being negative with clinical suspicion, HCV RNA should be checked. There is no vaccine yet to protect against HCV. For this reason, methods of preventing contagion have come to the fore (17). In our study, anti-HCV results of 18231 patients aged 0-18 years were evaluated, and it was positive in 11 (0.1%) children.

Two of these patients were positive for HCV RNA and were followed up in pediatric gastroenterology. There are a limited number of studies evaluating HCV seroprevalence in children in Turkey. The results of our study were similar to the anti-HCV seroprevalence; detected as 0.1% in the study by Doğan et al., 0.3% in the study by Deveci et al., 0.09% in the study by Güçlü et al., and 0.1% in the study by Ayvaz et al. (2, 28-30).

CONCLUSION

As a result, our study, in which our 10-year data were evaluated retrospectively, is sample size wise the largest hepatitis seroprevalence study conducted in Turkey. In addition, successful results of hepatitis A and hepatitis B vaccination were noticed in our study. Therefore, we recommend that the extended immunization program carried out in Turkey be continued meticulously, and prevention methods should always be followed for hepatitis C.

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Conflict of Interest: The authors declare that they have no competing interest.

Ethical approval: Approval of the study, dated 09.03.2022 and numbered 2022-KAEK-31, was obtained from the Ethics Committee of Kastamonu University Faculty of Medicine.

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