

# Epidemiologic Trends in Human Hepatitis A Virus Infection Stratified by Age between 2010 and 2018 in Cheonan, Korea

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Although studies on Hepatitis A virus (HAV) were crucial in the establishment of the HAV infection prevention programs, no systematic investigation into HAV has been conducted since 1999. We retrospectively analyzed the data between January 2010 to December 2018 from all the patients who underwent HAV antibody tests at the Dankook University Hospital Health Care Center. Data were collected from 56,204 individuals. Overall, 34,834 (62.0%) individuals from this cohort were positive for HAV antibodies and the annual rate of anti-HAV antibody positivity was highest in 2010 (68.5%) and lowest in 2013 (54.8%). The average decline in the antibody positivity rate was 0.62% per year, showing a statistically significant difference ( $p < 0.001$ ). In the over 40s age group, anti-HAV antibody positivity rates decreased from 89% in 2010 to 64% in 2018 ( $p < 0.001$ ), with an annual decrease of 3.1%. In the over 30s age group, it decreased from 48.2% in 2010 to 34.7% in 2018 ( $p < 0.001$ ), with an annual decrease of 1.82%. This study shows that the antibody positivity rate is decreasing across age groups but given that HAV infection poses more significant risks in older patients it is important to expand the evaluations of the current and future antibody positivity rates for HAV in various age groups.

**Keywords:** Epidemiological monitoring, human Hepatitis A Virus, immunological surveillance, viral antibodies, viral diseases

## Introduction

Hepatitis A is caused by the hepatitis A virus (HAV), and whose primary site of replication is the liver [1]. HAV transmission mainly occurs through the fecal-oral route. Insufficient sanitation and poor hygienic conditions lead to contamination of water and food, especially shellfish [2, 3]. Moreover, areas with an inadequate water supply and wastewater facilities and hygiene generally have high HAV prevalence [4–6]. In Korea, Hepatitis A was 867 in 2013, and it has continued to increase

until 2018 [7].

HAV infections occurring before the age of 6 years are usually asymptomatic and resolve spontaneously, resulting in the generation of antibodies. However, the severity of this disease increases with age [8], and in older patients, inflammatory hepatitis may lead to rapid deterioration in hepatic function and death.

Anti-HAV antibodies (IgG) are generated in 60–90% of individuals exposed to HAV. Hence, the rate of anti-HAV antibody positivity in an age group could indicate the infection pattern of hepatitis A virus by age [9, 10]. Due to the high economic growth in Korea that has resulted in improved living conditions and personal hygiene, the rate of anti-HAV antibody positivity in 20–30s young individuals has decreased from 60% to less

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than 10% over the past 25 years. Consequently, the risk of developing hepatitis A at an older age has increased [10].

Recent studies on hepatitis have focused on the genetics of hepatitis viruses. Moreover, epidemiological research has largely been restricted to hepatitis B and C with limited studies focusing on hepatitis A. No systematic investigation into HAV has been conducted since 1999, even though studies on hepatitis were crucial for establishing programs to prevent HAV infection. To this end, we examined the trend of total antibody tests in all ages for HAV at Dankook University Hospital Health Care Center in Cheonan, Korea, over a 9years period, from 2010 to 2018.

## Materials and Methods

### Study design and setting

We retrospectively analyzed data from all patients who underwent a total antibody test for HAV at Dankook University Hospital Health Care Center between January 2010 and December 2018 in Cheonan, Korea.

### Population

All patients at the hospital health center were included, irrespective of age or sex. Patients who did not undergo HAV total antibody testing were excluded.

### Variables

We conducted the study by setting the HAV total antibody test date, subject's age, sex, and antibody positivity as variables.

### Measurements

For the total antibody test, anti-HAV antibody levels (total) (i.e., IgM and IgG) were evaluated with an ADVIA Centaur immunoassay system (Siemens, USA) and the HAV total reagents (Siemens Healthcare Diagnostics, USA) using a competitive chemiluminometric immunoassay. Anti-HAV IgM levels were evaluated with the ADVIA Centaur system and the IgM HAV reagents (Siemens Healthcare Diagnostics) using an antibody capture microparticle chemiluminometric immunoassay. When deciding the positivity of the antibody, the cut-off for the reactivity of anti-HAV (total) was 20.0 IU (international unit)/L, and for anti-HAV IgM reactivity, a signal-to-cut-off value of 1.2 S/Co was considered.

### Ethical considerations

The present study was approved by the institutional review board (IRB) of the Dankook University (IRB Approval No: 2019-02-002).

### Statistical methods

Data were analyzed for the HAV total antibody test results using the R statistical program (version 3.3.3, Comprehensive R Archive Network; <https://www.r-project.org>) and presented as the means (with standard deviation) and medians (with range). The chi-square test was used to analyze categorical data.

## Results

The characteristics of the study cohort are summarized in Table 1. The mean  $\pm$  SD age of the 56,204 individuals was  $41.9 \pm 11.6$  years. Correct to 32,568 (57.9%) were men, and 34,834 (62%) had HAV antibodies (20,548 men and 14,286 women). The positivity rate was significantly higher in men than in women ( $p < 0.001$ ).

The annual rate of anti-HAV antibody positivity was highest in 2010 at 68.5% and lowest in 2013 at 54.8%. The rate of antibody positivity decreased by 0.62% per year on average, showing a statistically significant difference ( $p < 0.001$ ). The highest and lowest mean age of those positive for HAV antibodies was 45.0 years (in 2018) and 39.8 years (in 2013) (Table 2).

In the age-specific analysis, the average rate of antibody positivity was found to be highest in those 60s age group (99.9%), and lowest in those aged 10–29 years (16.7%) (Fig. 1). No significant change was observed in the rate of antibody positivity among those over 60 years of age during the 9-year period. However, among those in the 40s age group, this rate decreased from 89% in

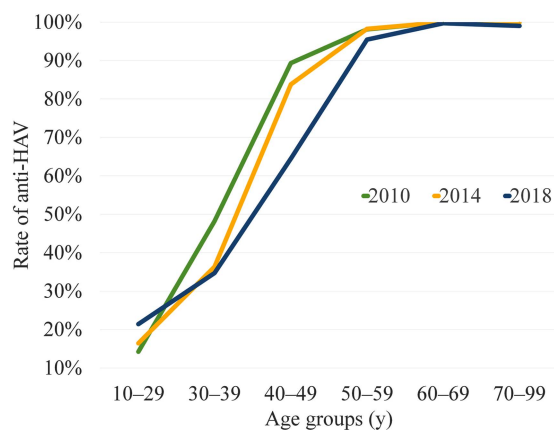
**Table 1. General characteristics of study participants.**

	Number	Proportion/ Rate	Average age (y) <sup>a</sup>
Total	56,204	100.0%	41.9
Male	32,568	57.9%	42.9
Female	23,636	42.1%	40.6
Positive	34,834	62.0%	47.2
Negative	21,370	38.0%	33.4

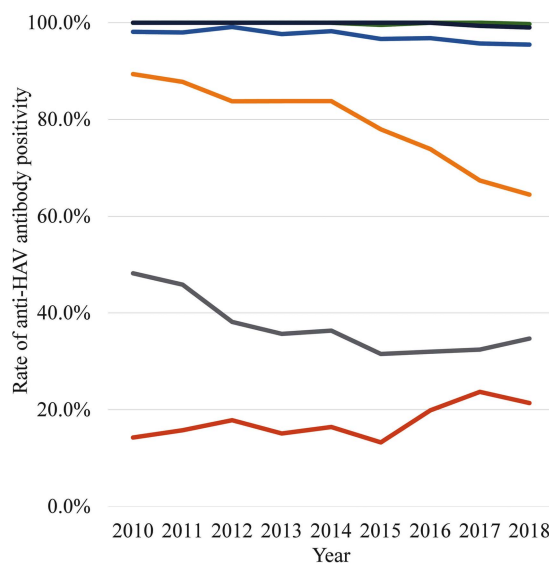
<sup>a</sup>Age range, 15.8–92.4 y

**Table 2. Prevalence of antibody positivity according to the year and age group.**

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	
No. of participants	11,153	9,275	5,571	7,972	4,961	5,392	4,382	4,187	3,311	
No. showing positive findings	7,639	6,116	3,308	4,369	2,993	3,189	2,673	2,494	2,053	
Rate of positivity	68%	66%	59%	55%	60%	59%	61%	60%	62%	
Average age (y)	41.2	41.5	40.9	39.8	41.6	43.3	44.3	44.0	45.0	
HAV antibody positivity rate according to age group	10-29 y	14%	16%	18%	15%	16%	13%	20%	24%	21%
	30-39 y	48%	46%	38%	36%	36%	32%	32%	32%	35%
	40-49 y	89%	88%	84%	84%	84%	78%	74%	67%	64%
	50-59 y	98%	98%	99%	98%	98%	97%	97%	96%	95%
	60-69 y	100%	100%	100%	100%	100%	100%	100%	100%	100%
	70-99 y	100%	100%	100%	100%	100%	100%	100%	99%	99%



**Fig. 1. Anti-HAV antibody positive rate according to age.** The age range is 15.8-82.3 and includes three years in this graph.



**Fig. 2. Anti-HAV antibody positive rate according to period with age group.** Each line represents anti-HAV antibody positive rate according to age group.

2010 to 64% in 2018 ( $p < 0.001$ ), with an annual decrease of 3.1%. Further, among those in the 30s age group, it decreased from 48.2% in 2010 to 34.7% in 2018 ( $p < 0.001$ ), with an annual decrease of 1.82% (Fig. 2).

## Discussion

In the study by Lee *et al.* [11], men accounted for 60% of those showing positivity for anti-HAV antibodies, and Ly *et al.* also [12] reported a significantly higher rate in men. This is consistent with our study, in which the rate of positivity was found to be 1.44-times higher in men. The prevalence of HAV has been reported to be influenced by socio-demographic factors such as residence, family size, and socioeconomic status [13], but further study is needed for differences in infection rates by gender.

This study analyzed the positivity rate of anti-HAV antibodies in a regional unit over time. In the present study, the mean age of participants was  $41.9 \pm 11$  years, higher than that in studies from Kim *et al.* [14], Laurence [15], and Ly *et al.* [12] (25, 33, and 36 years, respectively). This can be thought of as obtaining an anti-HAV antibody at an older age, when symptoms may be more severe. This result is thought to be due to the lower anti HAV antibody positivity rate in the relatively young age group of 10–39 years old.

The trend of annual antibody positivity showed a significant gradual decrease in our study, with the highest reduction observed among those in the 30s and 40s (decrease of 15% and 25%, respectively). This was similar to the findings of Lee *et al.* [16], who reported a downward trend in their 2009 study, and to those of Kim

*et al.* [17], who also reported a decrease in HAV antibody positivity rate among those in the 20s and 40s in their 2017 study.

The prevalence of hepatitis A varies according to living conditions, hygiene, and economic status. Infections have been reported to occur in children and adolescents in developing and developed countries, and in adults in developed countries [18]. In this study, the anti-HAV antibody positivity rate among those aged 10–29 years was lowest in 2015 (13%) and remained lower than 20% until 2018. In addition, it remained low at 35% among those in their 30s and 64% among those in their 40s, thus lowering the overall positivity rate from 68.5% to 54.8%. Kim *et al.* [19], in their 2006 report, predicted that teenagers and those in the 20s age would have an anti-HAV antibody positivity rate of less than 20%, and those in the 30s would have a prevalence of 70%.

Our study has some limitations. First, we collected a large size of data were sourced from a single center, our findings may not be representative of the real-life situation in Korea, and further analyses using data from multiple centers are warranted. Second, we could not determine whether the rate of HAV antibody positivity had reduced because of the decrease in incidence due to advances in the medical system because comparisons with the hepatitis A prevalence rate could not be made.

Wang *et al.* [20] reported an increase in the rate of antibody positivity due to active vaccination in China, and Sanguanmoo *et al.* [21] reported lower rates of anti-HAV antibody positivity in Thailand that have been reported in the past. Further, the severity of hepatitis A increases with age, and the disease may be fatal in older adults. Moreover, adults with hepatitis A may develop ectopic liver failure may or show an atypical clinical course, such as recurrent hepatitis, persistent hepatitis, or cholestatic hepatitis [22]. This study shows that the antibody positive rate by age group is decreasing. Since hepatitis A causes greater damage in adults, more extensive research is needed on the current and future positivity rates of HAV antibodies over time. We recommend hepatitis A vaccination in young adults to reduce the risk of HAV infection.

### Conflict of Interest

The authors have no financial conflicts of interest to declare.

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