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Factors associated with anti-hepatitis A virus immunoglobulin G seropositivity among Korean workers: a cross-sectional study

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ABSTRACT

Objectives Hepatitis A incidence in Korea has dramatically increased in recent years. Individuals in their twenties and thirties, who account for majority of the workforce in Korea, are particularly susceptible to infection owing to a low seroprevalence of anti-hepatitis A virus (anti-HAV) immunoglobulin G (IgG). This study aimed to identify behavioural and occupational factors related to anti-HAV IgG seropositivity.

Design Cross-sectional study.

Setting A large university hospital in Seoul, Korea.

Participants Workers in formal employment having an annual routine health screening.

Primary outcome measure Anti-HAV IgG seropositivity.

Results Of 131 711 individuals who had an annual health screening at the study hospital in 2018, 68 612 met the inclusion criteria and were included in the analysis. Study participants were predominantly men (64.3%) and in their thirties (55.3%). The overall seroprevalence of anti-HAV IgG was 36.2%. In multivariate analyses, anti-HAV IgG seropositivity was independently associated with working in a workplace with ≥2 health managers (vs no health manager, adjusted OR 1.32, 95% CI 1.22 to 1.43); age 40–49 years (vs 20–29 years, OR 2.51, 95% CI 2.36 to 2.68); female sex (OR 1.54, 95% CI 1.48 to 1.59); experience of any general disease (vs no general disease history, OR 1.19, 95% CI 1.14 to 1.25), obesity (vs normal weight, OR 0.91, 95% CI 0.86 to 0.97); and hepatitis B antibody seropositivity (OR 2.39, 95% CI 2.31 to 2.49).

Conclusions The low prevalence of anti-HAV IgG seropositivity points to a need for implementation of workplace-based hepatitis A vaccine programmes. To promote workers' health and prevent hepatitis A outbreaks, occupational health managers, healthcare providers and policy-makers should focus on individuals who are susceptible to HAV, such as young men.

Strengths and limitations of this study

- This study investigated a large sample size of 68 612 participants for cross-sectional analyses.
- We adjusted analyses for personal, behavioural and occupational factors drawn from clinical records.
- We obtained demographic data using a self-administered questionnaire so that there is possible information bias.
- The study findings were not generalised on other population groups since the study only included those in formal employment, most of whom were in Seoul and its suburb area in Korea.
- The study lacks the information of patients' vaccination history, and the cross-sectional nature of the study design makes it difficult to determine causal interference.

BACKGROUND

According to the WHO, hepatitis A caused an estimated 7134 deaths in 2016. Hepatitis A is a viral liver disease caused by hepatitis A virus (HAV). Globally, HAV infection occurs sporadically and as outbreaks. It is estimated that approximately 1.4 million people are infected each year.[1] Korea, one of the world's high-income countries, has very low HAV endemicity levels, and a high proportion of the population is susceptible to HAV infection.[2] There were 14 214 cases of hepatitis A reported to the Korea Centers for Disease Control and Prevention (KCDC) from 1 January to 6 September 2019, which is approximately 7.8 times the number of cases reported during the same period in 2018. KCDC attributed this increased incidence to the consumption of contaminated salted clam products and weak herd immunity among young Koreans.[3]

HAV transmission occurs when contaminated food or water is ingested (fecal-oral route) and via direct contact with an infectious person. Therefore, to prevent disease transmission, personal hygiene practices are very important. In addition, immunisation should be considered as a high priority. Immunity against HAV is acquired after

complete recovery from acute hepatitis A and when properly vaccinated.

Notwithstanding its relatively low mortality, epidemics of HAV can be prolonged and can result in substantial economic loss.[1] HAV vaccination was added to the National Immunization Program in 2015. Considering that young adults account for majority of the labour force in Korea and that HAV can cause outbreaks in communities with weak herd immunity, vaccination of young adults is of a great importance in workplace settings. However, vaccination coverage against HAV in Korea is low, and immunity may vary depending on personal and occupational factors.

This study aimed to determine the prevalence of anti-HAV immunoglobulin G (IgG) among Korean workers and identify behavioural or occupational factors associated with seropositivity.

METHODS

Study participants and setting, and sample size

We conducted a cross-sectional descriptive study. The source population comprised 131 711 individuals who underwent an annual health screening at Kangbuk Samsung Hospital in Seoul, Republic of Korea, between January and December 2018. The following individuals were excluded from the analysis: those who were not tested for anti-HAV IgG (n=54 552); those aged <20 (n=349) or ≥50 years (n=279) because of relatively smaller sample size than other age groups and the fact that people aged under 20 are not workers and that people aged more than 50 in South Korea are likely to have experienced HAV infection[4]; those without an occupation recorded (n=7128); those who were pregnant because we did not measure their waist circumference (n=775); and those with unmeasured total cholesterol (n=16). We included the remaining 68 612 workers in the analysis (figure 1).

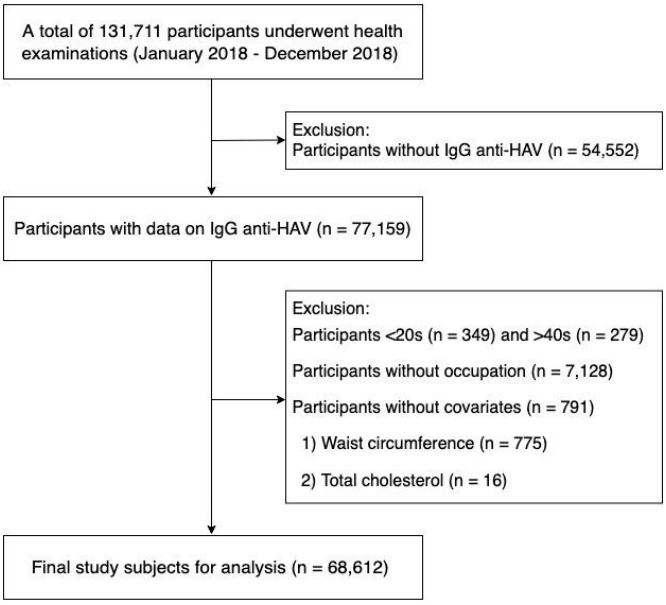

Figure 1 Flow chart of participant selection. HAV, hepatitis A virus; IgG, immunoglobulin G.

Measurement of variables

Data on age, sex, area of residence, occupation, general disease history, blood pressure, body mass index (BMI), waist circumference, fasting glucose, total cholesterol, presence of hepatitis B surface antibody (HBsAb) and anti-HAV IgG measured by automated chemiluminescence immunoassay were extracted from clinical records. General disease history such as stroke, cardiac disease, hypertension, diabetes, cancer, pulmonary tuberculosis, dyslipidaemia and any chronic or acute disease history were obtained through a doctor's face-to-face interview during health examination. Demographic data were obtained using a self-administered questionnaire. Clinical factors such as blood pressure, body weight and waist circumference were measured by trained nurses, and other blood parameters were measured using venous blood samples collected from antecubital vein after ≥12 hours of fasting.

Blood pressure was classified according to the Eighth Report of the Joint National Committee on Prevention.[5] BMI was divided into three categories: normal, <25 kg/m^2; overweight, 25–29.9 kg/m^2; and obese, ≥30 kg/m^2. Abdominal obesity was defined by waist circumference:>90 cm for men and >85 cm for women. Normal, glucose intolerance and suspected diabetes were defined as a fasting blood glucose level <100 mg/dL, 100–125 mg/dL and ≥126 mg/dL, respectively. A total cholesterol level ≥240 mg/dL was considered to be elevated.

In Korea, all workers are mandated to undergo an annual health examination. Occupational characteristics (Korean standard industrial classification and the number of workplace health managers) were collected by reviewing information documented at the time of the health examination.

Statistical analysis

The median and IQR were used to describe continuous variables with non-normal distributions, and the groups were compared using the Mann-Whitney U test. Normality test was accomplished using the Kolmogorov-Smirnov test. Categorical variables are expressed as percentages (%), and the groups were compared using χ^2 tests. Binary logistic regression was used to determine factors associated with IgG anti-HAV seropositivity and the results are expressed as ORs with 95% CIs. We performed bivariate logistic regression analysis, followed by forward-step adjustment. P values <0.05 were considered statistically significant. We used SPSS software (V.24.0; IBM) for the statistical analysis.

Patient and public involvement

As the study was retrospective and studied the workforce on a population level, rather than a specific group, there was no worker or public involvement in this research.

Table 1 Seroprevalence of anti-hepatitis A virus (HAV) immunoglobulin G (IgG) by participant demographic and clinical characteristics

	Total	IgG anti-HAV (+)	IgG anti-HAV (–)	P value
N (%)	68612 (100.0)	24871 (36.2)	43741 (63.8)	
Age (years), median (IQR)	32 (28–36)	33 (29–38)	31 (27–36)	<0.001
20–29, n (%)	24805 (36.2)	7236 (29.2)	17569 (70.8)	<0.001
30–39, n (%)	37959 (55.3)	14586 (38.4)	23373 (61.6)	
40–49, n (%)	5848 (8.5)	3049 (52.1)	2799 (47.9)	
Sex				
Male, n (%)	44151 (64.3)	14619 (33.1)	29532 (66.9)	<0.001
Female, n (%)	24461 (35.7)	10252 (41.9)	14209 (58.1)	
Residence				
Seoul city, n (%)	7526 (16.4)	3408 (45.3)	4118 (54.7)	<0.001
Gyeonggi-do, n (%)	27480 (59.8)	10682 (38.9)	16798 (61.1)	
Other regions, n (%)	10956 (23.8)	4062 (37.1)	6894 (62.9)	
Disease history (any)				
No, n (%)	59951 (87.4)	21105 (35.2)	38.846 (64.8)	<0.001
Yes, n (%)	8661 (12.6)	3766 (43.5)	4895 (56.5)	
Blood pressure (mm Hg)				
Normal, n (%)	31733 (46.2)	12193 (38.4)	19540 (61.6)	<0.001
Prehypertension, n (%)	34009 (49.6)	11679 (34.3)	22330 (65.7)	
Hypertension, n (%)	2870 (4.2)	999 (34.8)	1871 (65.2)	
BMI (kg/m^2), median (IQR)	24.1 (21.4–26.2)	23.9 (21.2–26.1)	24.2 (21.5–26.3)	<0.001
Normal, n (%)	44190 (64.4)	16399 (37.1)	27791 (62.9)	<0.001
Overweight, n (%)	19474 (28.4)	6752 (34.7)	12722 (65.3)	
Obese, n (%)	4948 (7.2)	1720 (34.8)	3228 (65.2)	
Waist circumference (cm), median (IQR)	80.3 (72.0–87.4)	79.7 (71.1–87.0)	80.6 (73.0–87.7)	<0.001
Normal, n (%)	55608 (81.0)	20308 (36.5)	35300 (63.5)	0.002
Abdominal obesity, n (%)	13004 (19.0)	4563 (35.1)	8441 (64.9)	
Fasting glucose (mg/dL), median (IQR)	92 (86–97)	93 (86–97)	92 (86–97)	0.002
Normal, n (%)	57487 (83.8)	20731 (36.1)	36756 (63.9)	0.02
Glucose intolerance, n (%)	10400 (15.2)	3852 (37.0)	6548 (63.0)	
Suspected diabetes, n (%)	725 (1.1)	288 (39.7)	437 (60.3)	
Total cholesterol (mg/dL), median (IQR)	187 (165–207)	187 (165–207)	187 (165–207)	0.91
Normal, n (%)	64414 (93.9)	23281 (36.1)	41133 (63.9)	0.02
Elevated, n (%)	4198 (6.1)	1590 (37.9)	2608 (62.1)	
HBsAb				
Negative, n (%)	23111 (33.7)	5099 (22.1)	18012 (77.9)	<0.001
Positive, n (%)	45501 (66.3)	19772 (43.5)	25729 (56.5)	

BMI, body mass index; HAV, hepatitis A virus; HBsAb, hepatitis B surface antibody; IgG, immunoglobulin G; IQR, interquartile range.

RESULTS

Characteristics of study participants and seroprevalence of anti-HAV IgG antibody

The study population comprised more men (64.3%) than women, and most of the study population were in their thirties (55.3%) and living in Gyeonggi-do (59.8%), a suburb area of Seoul. The participants were relatively healthy: 12.6% had a disease history. The prevalence of hypertension, obesity, diabetes and dyslipidaemia was 4.2%, 7.2%, 1.1% and 6.1%, respectively, and serology revealed that 66.3% of participants were HBsAb positive. None of the participants reported a history of hepatitis A. The overall seroprevalence of anti-HAV IgG (hereinafter seroprevalence) was 36.2%, and it differed significantly by sex, age, area of residence, disease history, blood pressure, BMI, total

Table 2 Seroprevalence of anti-hepatitis A virus (HAV) immunoglobulin G (IgG) and occupational characteristics of the study participants

	Total	IgG anti-HAV (+)	IgG anti-HAV (–)	P value
Occupational sector*				
Manufacturing, n (%)	61 405 (89.6)	22 042 (35.9)	39 363 (64.1)	<0.001
Construction, n (%)	1106 (1.6)	331 (29.9)	775 (70.1)	
Wholesale and retail trade, n (%)	1097 (1.6)	307 (28.0)	790 (72.0)	
Accommodation and food service activities, n (%)	328 (0.5)	101 (30.8)	227 (69.2)	
Information and communication, n (%)	1128 (1.6)	351 (31.1)	777 (68.9)	
Financial and insurance activities, n (%)	841 (1.2)	202 (24.0)	639 (76.0)	
Professional, scientific and technical activities, n (%)	713 (1.0)	234 (32.8)	479 (67.2)	
Business facilities management and business support services; rental and leasing activities, n (%)	179 (0.3)	63 (35.2)	116 (64.8)	
Education, n (%)	464 (0.7)	136 (29.3)	328 (70.7)	
Human health and social work activities, n (%)	1240 (1.8)	1043 (84.1)	197 (15.9)	
Workplace health manager				
No, n (%)	3196 (4.7)	948 (29.7)	2248 (70.3)	<0.001
Yes, n (%)	65 416 (95.3)	23 923 (36.6)	41 493 (63.4)	
Number of health managers				
0, n (%)	3196 (4.7)	948 (29.7)	2248 (70.3)	<0.001
1, n (%)	2967 (4.3)	1558 (52.5)	1409 (47.5)	
≥2, n (%)	62 449 (91.2)	22 365 (35.8)	40 084 (64.2)	

*Occupational classifications with <50 workers are not shown.
HAV, hepatitis A virus; IgG, immunoglobulin G.

cholesterol level, fasting blood glucose level and HBsAb status (table 1).

In terms of occupation, the majority of participants (89.6%) were working in the manufacturing sector. Seroprevalence was significantly different over all occupational classifications (p<0.001) and was the highest among participants involved in human health and social work activities (84.1%) and the manufacturing industry (35.9 %). Most workplaces had one or more health managers (95.3%). Seroprevalence was significantly higher among participants with ≥1 workplace health manager (36.6%) and was the highest for those with a single health manager (52.5 %; table 2).

Factors associated with the presence of antibodies to HAV

In the fully adjusted logistic regression model, age, sex, BMI, disease history, hepatitis B status, occupational classification and number of workplace health managers showed significant association with HAV seropositivity (table 3). Working in a workplace with ≥2 health managers (vs no health manager, adjusted OR 1.32, 95% CI 1.22 to 1.43); age 40–49 years (vs 20–29 years, OR 2.51, 95% CI 2.36 to 2.68); female sex (OR 1.54, 95% CI 1.48 to 1.59); and hepatitis B antibody seropositivity (OR 2.39, 95% CI 2.31 to 2.49) had relatively greater magnitude of associations compared with the other factors. Regarding the number of health managers, there was a trend towards a higher anti-HAV seroprevalence with an increasing number of workplace health managers (p for trend <0.001).

DISCUSSION

Principal findings

The overall seroprevalence of anti-HAV IgG was 36.2%, and was positively associated with age. Men and those living outside Seoul had a lower seroprevalence than women and those living in Seoul, respectively, and were thus more susceptible to HAV infection, while in the adjusted analysis those working in workplaces with the larger number of health managers were more likely to be anti-HAV IgG positive.

Prevalence of HAV immunity

According to WHO in 2009, the estimated prevalence of immunity against hepatitis A in Korea increased with age, from 25% among those aged 20–24 years to 66% among those aged 45–54 years.[6] In 2015, Korea National Health and Nutrition Examination Survey, a population-based survey of anti-HAV IgG seroprevalence of 5856 people revealed that the seroprevalence increased with age, from 12.6% among those aged 19–29 years to 80.3% among those aged 40–49 years.[4] Our study results were closer to the WHO estimates. The variation in seroprevalence using surveys is likely because of the different conditions and time points at which the surveys were conducted,

Table 3 Factors associated with anti-hepatitis A virus seropositivity

	Crude	Adjusted ORs
Age (years)		
20–29	1.00 (reference)	1.00 (reference)
30–39	1.52 (1.46 to 1.57)	1.32 (1.27 to 1.37)
40–49	2.65 (2.50 to 2.80)	2.51 (2.36 to 2.68)
Sex		
Male	1.00 (reference)	1.00 (reference)
Female	1.46 (1.41 to 1.51)	1.54 (1.48 to 1.59)
Residence*		
Other regions	1.00 (reference)	
Gyeonggi-do	1.08 (1.03 to 1.13)	
Seoul city	1.41 (1.32 to 1.49)	
Disease history (any)		
No	1.00 (reference)	1.00 (reference)
Yes	1.42 (1.35 to 1.48)	1.19 (1.14 to 1.25)
Blood pressure		
Normal	1.00 (reference)	
Prehypertension	0.84 (0.81 to 0.87)	
Hypertension	0.86 (0.79 to 0.93)	
BMI		
Normal weight	1.00 (reference)	1.00 (reference)
Overweight	0.90 (0.87 to 0.93)	0.94 (0.90 to 0.97)
Obese	0.90 (0.85 to 0.96)	0.91 (0.86 to 0.97)
Waist circumference		
Normal	1.00 (reference)	
Abdominal obesity	0.94 (0.90 to 0.98)	
Fasting glucose		
Normal	1.00 (reference)	
Glucose intolerance	1.04 (1.00 to 1.09)	
Suspected diabetes	1.17 (1.01 to 1.36)	
Total cholesterol		
Normal	1.00 (reference)	
Elevated	1.08 (1.01 to 1.15)	
HBsAb		
Negative	1.00 (reference)	1.00 (reference)
Positive	2.72 (2.62 to 2.82)	2.39 (2.31 to 2.49)
Occupational classification		
Others	1.00 (reference)	1.00 (reference)
Human health and social work activities	9.68 (8.30 to 11.28)	9.07 (7.52 to 10.93)
Workplace health manager		
No	1.000 (reference)	
Yes	1.37 (1.27 to 1.48)	
Number of health managers		
0	1.00 (reference)	1.00 (reference)
1	2.62 (2.36 to 2.91)	1.04 (0.91 to 1.18)
≥2 or more	1.32 (1.22 to 1.43)	1.32 (1.22 to 1.43)†

*Residence was not considered when adjustment due to missing values.
†P for trend <0.001.
BMI, body mass index; HBsAb, hepatitis B surface antibody.

although there was a consistent trend toward increasing anti-HAV IgG seroprevalence across all surveys.[4 6] This trend seems to have been due to the decrease in exposure to the HAV of the lower age groups due to the high economic growth and improvement of public health and living conditions in Korea over the past decades.

Related factors

In our study, women had significantly higher seroprevalence of anti-HAV IgG than men. In Korea, a survey of the national influenza vaccination rate revealed that the rate was higher among women than among men, and it is well known that there are biological differences in response to vaccination according to sex.[7 8] In our study, the difference in anti-HAV IgG seroprevalence is also likely because of the behavioural and biological differences according to sex although we could not present vaccination history directly. Geographically, most participants resided in urban areas, and those who lived in Seoul were more likely to be immune to HAV than those who lived in other regions. This difference may be owing to better access to medical care in Seoul so that lower barriers to health behaviour; however, the National Health and Nutrition Survey in Korea did not determine a significant difference in anti-HAV IgG seroprevalence between rural and urban areas.[9]

We tried to identify clinical factors that could be used as surrogates of associations between personal behaviour and HAV immunity because several studies have shown that health behaviours were related to vaccination behaviours as well as medication adherence, management of hypertension and hyperlipidaemia, and dysfunctional health beliefs about obesity,[10] although no previous published studies have directly proved the relationship

between personal behaviour and hepatitis A vaccination yet. Indeed, anti-HAV seroprevalence differed significantly by disease history, blood pressure, BMI, waist circumference, total cholesterol level and fasting blood glucose, suggesting that these factors presumably due to health behaviours related to vaccination rather than clinical or pathological mechanism and among them, disease history and BMI were significantly associated even after adjustment. HBsAb seropositivity was also significantly associated even after adjustment, and this result is understandable because the factor is associated with medical service utilisation. Most importantly, our study demonstrated distinctive difference in anti-HAV IgG seroprevalence with respect to occupational classification and a significant association between the presence of workplace health managers and anti-HAV IgG seroprevalence. In this study, most participants involved in the occupational category of health and social work activities were hospital workers. This higher seroprevalence among hospital workers may be because of the recent HAV epidemics in Korea, which resulted in immunisation campaigns to protect high-risk population such as healthcare providers. In Korea, occupational safety and health acts mandate companies to employ health managers to promote workers' health; however, the required number varies by size and classification of the business. One of the main duties of health managers is to review the results of regular health examinations and to implement workplace health policies. The positive trend between the number of workplace health managers and anti-HAV seroprevalence in our study suggests the importance of their role. In contrast, workers working for small businesses (without health managers, or with too few health managers) might not be protected against HAV epidemics.

Strengths and limitations

This study aimed at a group of healthy young Korean workers, the majority of whom were working for multinational corporations. The limitations of the study were as follows: first, its cross-sectional design assess the exposure and outcome simultaneously, so that it makes it difficult to determine temporal causality and there is a need for further longitudinal studies. Second, it was unknown whether hepatitis A IgG antibody seropositivity of participants was acquired by vaccination or past infection because of the absence of records on vaccination history in our study. Third, demographic data such as residence were obtained by self-administered questionnaire so that it may cause possible information bias. Fourth, despite the large sample size, the results may not be generalisable to the whole of the Korean workforce because the study was conducted at only one hospital that does health screening for individuals, most of whom were working in Seoul or its suburb area, and it did not include people in informal employment. Nevertheless, the study reveals several statistically significant associations even after adjustment and provides valuable information about workers who might be vulnerable to HAV infection.

Recommendation

WHO guidelines state that planning for large-scale immunisation programmes should involve careful economic evaluations; therefore, we need to place higher priority on vulnerable and high-risk groups.[1] Further research is required on gender differences in HAV vaccination uptake, and studies with better designs, such as prospective cohort studies are required to illuminate causal relationships between the presence of workplace health managers and workers' health.

CONCLUSION

When preparing immunisation programmes, healthcare providers and policy-makers should consider the related factors, and place higher priority on immunising the most susceptible workers such as young men.

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Competing interests None declared.

Patient consent for publication Not required.

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