

A Survey of the Knowledge of and Testing Rate for Hepatitis C in the General Population in South Korea

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Background/Aims: To eliminate hepatitis C virus (HCV) infection, improving public knowledge of and access to HCV screening and treatment is essential. The aim of this study was to evaluate the knowledge of and testing rate for HCV and the opinions about the inclusion of the HCV test in the National Health Examination (NHE) among the general population in South Korea. **Methods:** A telephone interview survey was conducted by an independent research company using a 16 item-questionnaire (demographics, knowledge of HCV, testing and results, need for screening) in May 2019. The sample population consisted of 1,003 adult Korean residents adjusted by age, sex, and area according to the standard Korean population in 2019. **Results:** Among the 1,003 participants (505 women, mean age of 47.9 years), 56.4% recognized HCV; 44.4% understood that HCV is transmittable, and 56.8% thought that HCV is curable by medication. The recognition rate tended to increase with an increasing level of education. Testing for anti-HCV antibodies was reported by 91 people (9.1%); among them, 10 people (11.0%) reported a positive result, and eight people received treatment. The common reasons for HCV testing were a health check-up (58.5%), a physician's recommendation (11.0%) and elevated liver enzyme levels (10.7%). The majority of the population (75.1%) agreed with the integration of HCV into the NHE. **Conclusions:** The level of knowledge of HCV is suboptimal, and the self-reported testing rate for HCV is less than 10%; however, once HCV infection is diagnosed, the treatment rate seems to be high in South Korea. More active campaigns and effective screening are needed. (**Gut Liver 2020;14:808-816**)

Key Words: Hepatitis C, chronic; Awareness; Knowledge; Transmission; Public health

INTRODUCTION

Hepatitis C virus (HCV) infection is a major public health concern because of its disease burden and communicability. Globally, approximately 71 million people have been infected with HCV, which could lead to liver cirrhosis and hepatocellular carcinoma. In 2015, HCV-related mortality was 400,000 per year showing an increasing number from 200,000 deaths in 2000, which is in contrast to the decreasing trend of mortality from HIV (human immunodeficiency virus), tuberculosis and malaria.^{1,2}

Patients with hepatitis C can be easily screened with an anti-HCV test, and more than 90% of the patients are easily cured from a HCV infection with oral direct acting antiviral (DAA) therapy for 8 to 12 weeks,^{3,4} which stops the disease progression to liver cirrhosis and reduces the risk of hepatocellular carcinoma development.⁵⁻⁸ Considering that most of the mortality and medical cost was attributable to complications from liver cirrhosis and hepatocellular carcinoma, early diagnosis and treatment of HCV are a very important issue for promoting the public health. In this background, the World Health Organization has recently drafted a set of hepatitis elimination targets, which include a 65% reduction in HCV-related deaths and a 90% reduction in HCV incidence by 2030.²

In the era of DAA, under-diagnosis and gaps in linkage to care are the major barrier to the elimination of HCV. According to 2017 World Health Organization Global Hepatitis Report, only 20% of HCV, infected people are aware of their infection globally.⁹ However, the awareness rate was less than 10% in South-East Asia,¹⁰ where hepatitis B virus, not HCV, has been the major cause of liver-related mortality, and HCV was less recognized by the general population. Though public knowledge, awareness, attention and action are critically important

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to make a successful elimination strategy, there are only a few studies on the public knowledge and screening rate of HCV in East Asian countries. In South Korea, where the anti-HCV prevalence is 0.7%, no effective HCV screening program is operating yet. Therefore, the aims of this study were to evaluate the knowledge and self-reported testing rate of HCV and to assess public opinion about HCV screening among the general population of South Korea in 2019.

MATERIALS AND METHODS

1. Sampling procedure and telephone survey

The telephone interview survey was conducted by trained interviewers from a professional survey company (Gallup Korea, Seoul) in May 2019. A nationwide random sample of telephone numbers was obtained to conduct the survey. These telephone numbers were randomly selected from eight provinces of South Korea based on a per capita ratio using a random digit-dialing program which is the gold standard methodology for control recruitment in population-based epidemiologic research.^{11,12} The ratio of fixed-line and cordless calls was 20:80 and weighted by sex, age, and area based on the resident registration population from the Ministry of the Interior and Safety at the end of January 2019.¹³ A sex-, age-, and area-random sample of 1,003 respondents, aged more than 19 years, was obtained.

All telephone contacts were tracked and recorded on a database. Before the telephone interview, the interviewer explained to all eligible individuals the purpose of the study and requested their participation. Respondents gave informed verbal consent before the survey, and all respondents were interviewed by telephone survey interviewer. The response rate was 17%, and this survey had a margin of error of $\pm 3.1\%$ point at a 95% level of confidence.

This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (IRB number: X-1905/543-901).

2. Questionnaire

The questionnaire contained 16 questions including five demographic questions (age, sex, resident area, education level, and monthly income), five knowledge and five testing state questions and one public opinion question about HCV shown below. The Korean version of the questionnaire form used in this study is presented in Supplementary Fig. 1.

Part 1 Questions: Knowledge of hepatitis C in the general population; (1) Have you ever heard about HCV? (2) Do you think HCV is transmittable? (3) Can HCV be transmitted by tattooing, syringe use or acupuncture? (4) Should hepatitis C patients use separate dishes or towels from others? (5) Do you think HCV can be cured with drug therapy?

Part 2 Questions: Testing state of hepatitis C in the general population; (1) Have you ever been tested for anti-HCV? (2)

Why did you get tested for anti-HCV? (3) What was the test result? (4) If you were diagnosed with hepatitis C, did you get treatment? (5) If you were treated, what type of drugs were you prescribed (injection type drug or all oral drugs)?

Part 3 Question: Public opinion about HCV screening among the general population; Do you think anti-HCV testing should be included in the National Health Examination?

3. Statistical analysis

Tables were constructed for frequency and percentage. The baseline characteristics of the subjects were compared by the chi-square test for categorical variables, and the t-test was used to compare continuous variables. All p-values were two-sided, and <0.05 was considered significant. The SPSS version 21 (IBM Corp., Chicago, IL, USA) software was used for the statistical analyses.

Post-stratification weighting adjustment was applied to make the weighted records represent the population of inference as closely as possible.¹⁴ The post-stratification variables included sex (male/female), five age groups (19–29, 30–39, 40–49, 50–59, and ≥ 60 years), and eight census regions (Seoul, Incheon/Gyeonggi, Gangwon, Daejeon/Sejong/Chungcheong, Daegu/Gyeongbuk, Busan/Ulsan/Gyeongnam, Gwangju/Jeolla, and Jeju). Because the study sample sizes were typically too small to accommodate a complete cross-tabulation of all the survey variables with the benchmark variables, an iterative proportional fitting was used for the post-stratification weighting adjustment. This procedure adjusted the sample data back to the selected benchmark proportions. Through an iterative convergence process, the weighted sample data were optimally fitted to the marginal distributions.

RESULTS

1. Characteristics of the study population

The study population consisted of a random sample of 1,003 South Korean residents aged more than 19 years, who were stratified by age, sex and geographic difference. The mean age of the patients was 47.9 years with a male proportion of 49.6%, and 54% had an education level of a college degree or higher. The general characteristics of the study population before and after the adjustment are shown in Table 1.

2. Knowledge status on HCV among the general population

Among the 1,003 respondents, 56.4% heard of hepatitis C, which was classified as the HCV recognition group (Fig. 1). The recognition rate tended to increase from the 20s to the 50s and then decrease. While the HCV recognition rate showed no significant difference according to sex or geographic region, it tended to increase according to the increasing level of education and average household income, though it was not statistically significant: 80.4% in the high education group over a master's

Table 1. Baseline Characteristics of the Study Subjects

Characteristic	Study subjects	Adjusted subjects*	Whole adult South Korean
No.	1,003	1,003	43,044,713
Male sex	497 (49.7)	497 (49.6)	21,334,875 (49.6)
Age, yr	49.6±17.4	47.9±17.0	
19–29	174 (17.4)	174 (17.4)	7,438,522 (17.3)
30–39	168 (16.8)	168 (16.8)	7,247,690 (16.8)
40–49	196 (19.6)	196 (19.6)	8,484,276 (19.7)
50–59	203 (20.2)	202 (20.2)	8,629,296 (20.0)
60–69	139 (13.9)	139 (13.9)	5,978,518 (13.9)
70–79	89 (8.8)	89 (8.8)	3,505,803 (8.1)
≥80	34 (3.4)	34 (3.4)	1,760,608 (4.1)
Residence area			
Seoul	200 (19.9)	194 (19.4)	8,335,109 (19.4)
Incheon/Gyeonggi	303 (30.2)	306 (30.5)	13,111,906 (30.5)
Gangwon	30 (3.0)	30 (3.0)	1,299,071 (3.0)
Daejeon/Chungcheong	105 (10.5)	106 (10.5)	4,534,192 (10.5)
Daegu/Gyeongbuk	100 (10.0)	100 (10.0)	4,302,165 (10.0)
Busan/Ulsan/Gyeongnam	152 (15.2)	155 (15.4)	6,644,809 (15.4)
Gwangju/Jeolla	100 (10.0)	100 (9.9)	4,278,825 (9.9)
Jeju	13 (1.3)	13 (1.3)	538,636 (1.3)
Education level			
≤Elementary school	88 (8.7)	88 (8.7)	-
Middle school	68 (6.8)	68 (6.8)	-
High school	272 (27.2)	272 (27.2)	-
University	495 (49.4)	495 (49.4)	-
Graduate school	46 (4.6)	46 (4.6)	-
Refuse to respond	34 (3.4)	34 (3.4)	-
Average monthly income, USD*			
<1,275	147 (14.7)	147 (14.7)	-
1,275–2,550	162 (16.1)	162 (16.1)	-
2,550–3,400	147 (14.7)	147 (14.7)	-
3,400–4,675	154 (15.4)	154 (15.4)	-
4,675–7,225	119 (11.8)	119 (11.8)	-
≥7,225	73 (7.2)	73 (7.2)	-
Refuse to respond	201 (20.0)	201 (20.0)	-

Data are presented as number (%) or mean±SD. Weighted by sex, age, and area based on the resident population registered with the Ministry of the Interior and Safety at the end of January 2019.¹³

USD, United States dollar.

*Based on South Korea Won to the USD exchange rate on July 12, 2019.

degree and 77.3% in the high-income group over 4,675 to 7,225 USD (United States dollars) per month. However, the HCV recognition rate was low among the highest income class (≥7,225 USD/month).

Among the 1,003 respondents, 44.4% thought HCV is transmittable. After a suggestion that HCV is a communicable disease, 69.8% agreed to a parenteral route of transmission such as contamination from tattooing, syringe use or an acupuncture

procedure. However, 55.2% thought that HCV patients should use separate dishes or towels from others, which suggested fecal to oral transmission or by casual contact. Moreover, 56.8% answered that HCV can be cured by adequate medication (Fig. 2).

The HCV recognition group generally had better knowledge compared to the HCV non-recognition group (Supplementary Table 1). The acquisition of correct knowledge about HCV tended to be lower in the people in their 60s or older, low level

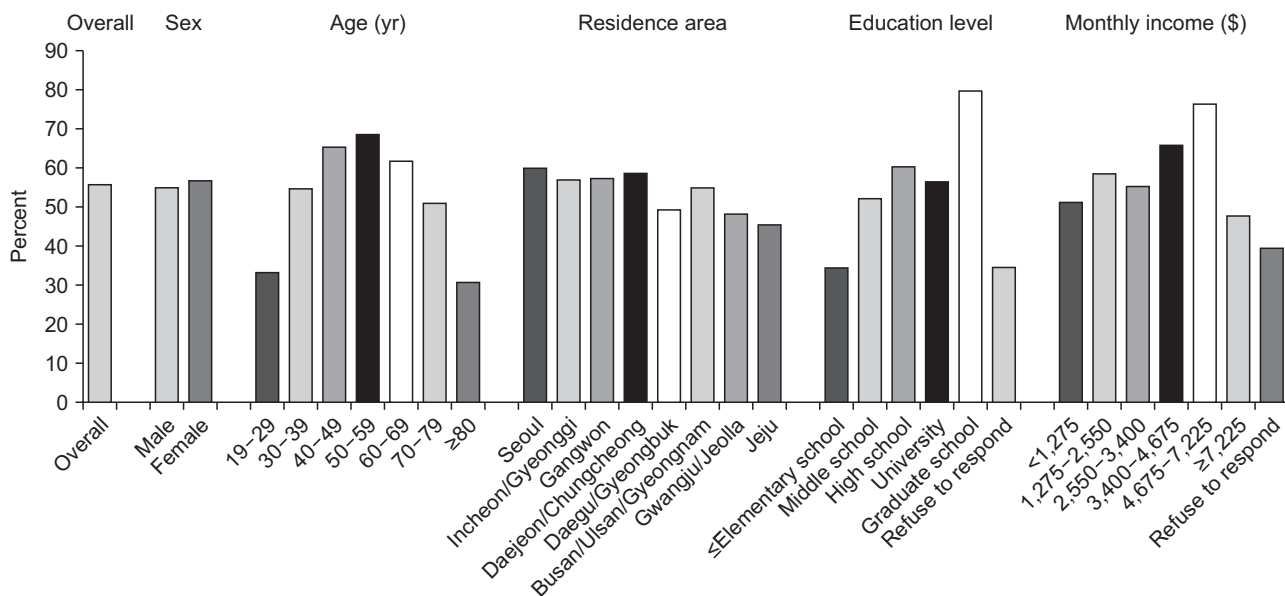


Fig. 1. Recognition rate of hepatitis C virus (HCV) among the general population of South Korea in 2019: positive response to the question “Have you ever heard about HCV?” Among the 1,003 survey respondents, 56.4% had heard of hepatitis C. The recognition rate tended to increase from respondents in their 20s to those in their 50s and then decrease. While the HCV recognition rate showed no significant difference according to sex or geographic region, it tended to increase with increasing levels of education and average household income, though the associations were not statistically significant. Margin of error: ±3.1% (95% confidence interval).

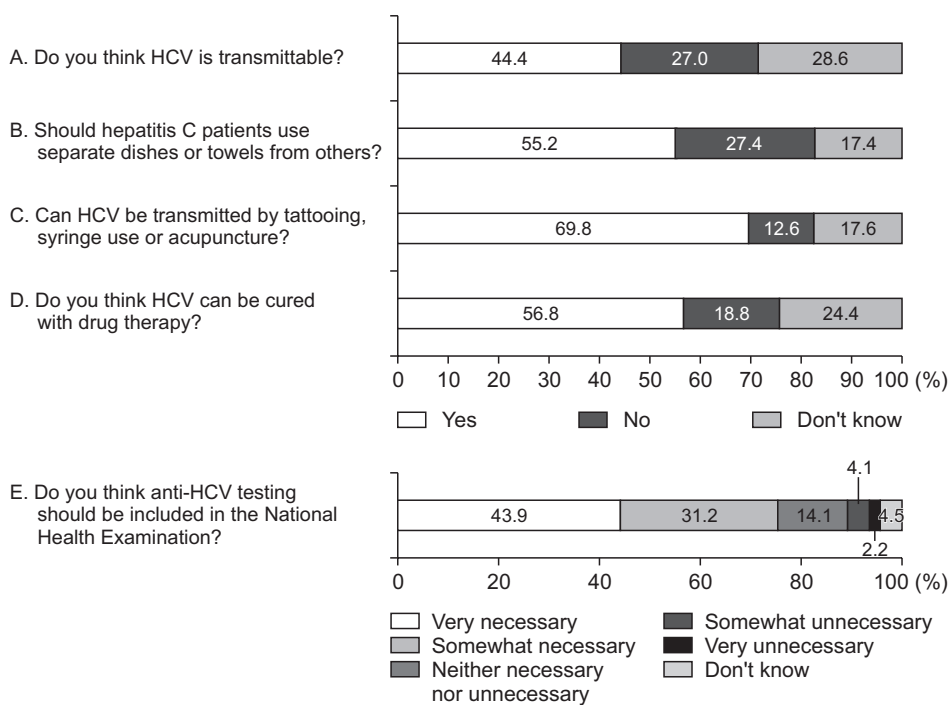


Fig. 2. The knowledge of hepatitis C virus (HCV) and opinions about the inclusion of the HCV test in the National Health Examination. Among the 1,003 respondents, 44.4% thought HCV is transmittable, 69.8% thought there was a parenteral route of transmission, and 56.8% believed that HCV can be cured by adequate medication. The majority of respondents (75.1%) agreed that an anti-HCV test should be included as a basic item in the National Health Examination. Margin of error: ±3.1% (95% confidence interval).

of education (below middle school degree), and lowest monthly income (<1,275 USD), and living in the Gwangju/Jeolla area (Table 2, Supplementary Tables 2-5). The Gwangju/Jeolla area had the second highest mean age and the second lowest college graduate rate and monthly income among the eight areas.

3. Self-reported HCV testing rate and its result in the Korean general population

Among the 1,003 subjects, 91 (9.1%) reported that they had received an HCV test (Fig. 3A). The reasons why they had undergone HCV testing were health check-up (58.5%), physician’s recommendation (11.0%), elevated liver enzymes (10.7%), ac-

Table 2. Self-Reported HCV Testing Rate in the General Korean Population Stratified by Subgroup

Subgroup	No.	Exam rate, %	p-value
Overall	1,003	91 (9.1)	-
Sex			0.34
Male	498	50 (10.0)	
Female	506	42 (8.3)	
Age, yr			0.02
19–29	174	4 (2.3)	
30–39	168	19 (11.3)	
40–49	196	18 (9.2)	
50–59	203	23 (11.3)	
60–69	140	18 (12.9)	
70–79	89	8 (9.0)	
≥80	34	2 (5.9)	
Residence area			0.76
Seoul	196	19 (9.7)	
Incheon/Gyeonggi	306	31 (10.1)	
Gangwon	30	2 (6.7)	
Daejeon/Chungcheong	106	11 (10.4)	
Daegu/Gyeongbuk	101	7 (6.9)	
Busan/Ulsan/Gyeongnam	155	16 (10.3)	
Gwangju/Jeolla	100	6 (6.0)	
Jeju	13	0	
Education level			0.19
≤Elementary school	87	5 (5.7)	
Middle school	68	5 (7.4)	
High school	272	25 (9.2)	
University	495	45 (9.1)	
Graduate school	46	9 (19.6)	
Refuse to respond	34	3 (8.8)	
Average monthly income, USD*			0.16
<1,275	147	14 (9.5)	
1,275–2,550	161	12 (7.5)	
2,550–3,400	147	9 (6.1)	
3,400–4,675	155	17 (11.0)	
4,675–7,225	118	18 (15.3)	
≥7,225	73	7 (9.6)	
Refuse to respond	201	14 (7.0)	

Weighted by sex, age, and area based on the resident population registered with the Ministry of the Interior and Safety at the end of January 2019.¹³

HCV, hepatitis C virus; USD, United States dollar.

*Based on South Korea Won to the USD exchange rate on July 12, 2019.

quaintances' advice (9.3%), family history of liver disease (8.0%) and exposure in mass media (3.5%) (Fig. 3B). The HCV testing rate was significantly low in the young age group with those in their

20s, but the people in their 30s and above had a similar testing rate from 9% to 12.9% according to increasing age (Table 2, Fig. 3).

4. Treatment pattern among the respondents with a positive anti-HCV test

Among the 91 testing people, 10 (11.0%) were reported that their anti-HCV testing result was positive: seven men and three women. Based on geographic distribution, there were two (1.0%) in Seoul, two (0.7%) in Incheon/Gyeonggi, four (3.8%) in Daejeon/Chungcheong/Sejong, two (2.0%) in Gwangju-Jeolla, one (0.6%) in Busan/Ulsan/Gyeongnam, Gangwon and 0 in Daegu/Gyeongbuk, and Jeju. The reasons for the anti-HCV testing were health check-up (n=4), elevated liver enzyme (n=4), and physician's recommendation (n=2). Among the 10 anti-HCV positive people, five were treated with an injection type drugs (probably pegylated interferon-based regimen) and three with all oral drugs. Interestingly, only four among the 10 respondents thought HCV is transmittable.

5. Necessity of HCV antibody test for nationwide health check-up

Though the information that the prevalence of hepatitis C in South Korea is less than 1% was given to the participants, 75.1% (very necessary 43.9% and somewhat necessary 32.2%) agreed that an anti-HCV test should be included as a basic item for the National Health Exam (Fig. 2). In particular, people in their 50s to 70s had a high agreement rate of over 80%. All subgroups had a high favor rate of over 70% regardless of the geographic region and average household income (Supplementary Table 6).

DISCUSSION

In this telephone interview survey study, 56.4% of the general population of South Korea recognized HCV, 44.4% understood HCV is transmissible, and 56.4% thought HCV is curable by medication. Recognition of HCV was highest in the age group of 50s and 60s, while knowledge on HCV was highest in the 20s. Testing an HCV test was reported in 91 people (9.1%), in them, 10 people (11.0%) reported as anti-HCV positive, and eight were treated. The major reason of HCV testing was health check-up (58.5%), and majority (75.1%) agreed to HCV screening by integration into National Health Examination system.

In South Korea, the anti-HCV prevalence adjusted for age, sex, and area among 291,314 health examinees (≥20 years of age) was 0.78% in 2009 and 0.6% in 2015.^{15,16} The anti-HCV prevalence increased with age, and it was higher in females (0.83%) than in males (0.75%), showing intranational geographic difference: a higher prevalence (1.53% to 2.07%) in the southern coastal area. More than 90% of Korean patients with chronic HCV infection were over 40 years of age, and more than half of the patients were asymptomatic or showing alanine

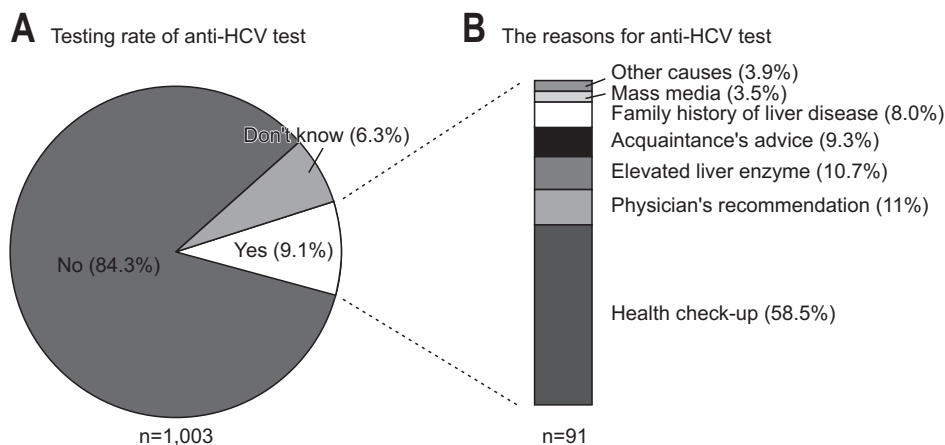


Fig. 3. Self-reported hepatitis C virus (HCV) testing rate and reasons for testing in the Korean general population in 2019. (A) Testing rate with the anti-HCV test. Testing for anti-HCV was reported by 91 people among the 1,003 survey subjects (9.1%). (B) The reasons for receiving the anti-HCV test. The common reasons for HCV testing were a health check-up (58.5%), a physician's recommendation (11.0%) and elevated liver enzyme levels (10.7%). Margin of error: $\pm 3.1\%$ (95% confidence interval).

aminotransferase levels within normal limits at their diagnosis of chronic hepatitis C. The major HCV genotypes are 1b (48%) and 2 (46%).¹⁷ It was reported that a one-time HCV screening and DAA treatment of the Korean population aged 40 to 65 years would be highly cost-effective and significantly reduce the HCV-related morbidity and mortality (incremental cost-effectiveness ratio of 7,435 USD compared with no screening).^{18,19} However, the anti-HCV test is not integrated in the National Health Examination system yet, which is the most efficient way of achieving HCV screening in Korea.

It is interesting that HCV is still recognized only in half of the adult population because two episodes of a HCV outbreak in two local clinics were extensively reported in the media in 2015²⁰ and 2017, respectively, and even one doctor at a clinic committed suicide during an investigation into the outbreak. The recognition rate tends to increase according to age, geographic region, and increasing level of education and income. The low prevalence of anti-HCV (0.34%) in the young adult group (<30 years) and in the Jeju area (0.26%) in 2009 may be an explanation, and generally, a high education level and income were related to a high awareness and knowledge of diseases including HCV.²¹⁻²³ In terms of treatment, 57% of people thought HCV is curable with medication, which is far below the 95% of the real life efficacy of DAA, recently.

For the knowledge about HCV, 56% of the people did not know HCV is communicable, and 70% of the people thought HCV patients should use separate dishes and towels, which suggests that the majority of the people consider HCV to be transmitted by casual contact or food. These prejudices may socially alienate HCV patients; therefore, widely spreading accurate knowledge is important not only for the prevention of HCV infection but also for the protection of HCV patients, socially.

This study is the first survey conducted in a representative population adjusted for the sex, age, and residence area of the population of South Korea, regarding the knowledge and HCV testing rate of HCV. Previously, there were three survey results on the knowledge of HCV in Korea: two online surveys in the

general population and one face-to face survey for health check examinees, all of which did not include people aged over 70 years, with a much smaller number of questions than in this study, and were not published in academic journals but reported to public media (Table 3). In addition, the relative strength of the phone survey in this study compared to online surveys is the interactive communication between the interviewer and respondent.²⁴

Despite the methodological difference of the above three surveys compared to the one in this study, the self-reported testing rate of anti-HCV in this study (9%, n=91) was quite similar to the previous survey results (10% to 12%), showing that the HCV screening rate has not improved during the recent 6 years (Table 3). However, South Korea has a welfare system called the National Health Examination, which is effective for early detection of diseases including five major cancers and metabolic diseases (diabetes and dyslipidemia). Though hepatitis B virus surface antigen and antibody tests are included in the National Health Examination, which are fully paid by the national health insurance, the anti-HCV test is not included in the National Health Examination yet. In this study, 75% of the population agree that the HCV screening test should be included in the National Health Examination system; moreover, 82% of health check examinees in the other survey also agreed to its inclusion in the National Health Examination, which was supported by several cost-effectiveness studies already published.^{18,25,26}

In this study, the anti-HCV positive rate among the respondents was unexpectedly high (11.0%, 10/91) considering that current anti-HCV prevalence among the Korean adult population of 0.6% to 0.8%.^{15,16} It may be related to the inherent limitation of telephone survey and its low response rate. In our study, the response rate of the telephone survey was 17%, however, it was a relatively higher rate compared to those in the other surveys on many political or economic issues: general response rate in telephone survey is within the range of 10% to 20% according to Gallup Korea. Moreover, anti-HCV test-

Table 3. Comparison of the Survey Results Regarding HCV in South Korea

Survey	Year			
	2019	2017	2016	2013
Survey method	Telephone	Face-to-face	Online	Online
Subjects	General population weighed by sex, age, and region	Health examinee	General population weighed by sex, age, and region	General population weighed by sex, age, and region
Age, yr	19–90	>20	20–59	14–69
No.	1,003	600	2,000	3,000
Have you ever heard about HCV?	56.4	-	76	-
Do you think HCV is transmittable?	44.4	-	-	-
Should hepatitis C patients use separate dishes or towels from others?	55.2	-	16–38	63.1
Can HCV be transmitted by tattooing, syringe use or acupuncture?	69.8	-	66	-
Do you think HCV can be cured with drug therapy?	56.8	44	-	82.3
Do you think anti-HCV testing should be included in the National Health Examination?	75.1	82	-	-
Have you ever tested anti-HCV?	9.1	10.4	12.2	10.4
Why did you test anti-HCV?	Health check-up (58.5) Physicians' recommend (11) Elevated liver enzyme (10.7) Acquaintances' advise (9.3) Family history of liver disease (8.0)	-	-	-
Self-reported positive rate of anti-HCV among HCV testing people	10.9	-	12.7	15.4
Self-reported positive rate of anti-HCV among the total subjects	1.0	-	1.6	1.6
Treatment rate among the self-reported anti-HCV positive people	80	-	65	-

The answer to the question was expressed in percent.
HCV, hepatitis C virus.

ing may be incorporated with other blood tests during routine health examination, in the workplace or a visit to clinic, which may not notify the participants. Therefore, anti-HCV testing rate may be underestimated, because it only depends on the respondent's report. In addition, recall bias may contribute either to underestimated anti-HCV testing rate or overestimation of the positive rate of anti-HCV. For example, 91 tested subjects may have more interest in or risk factors for HCV infection than the remaining non-tested group, which may result in a high anti-HCV positive rate.

Interestingly, among the 10 anti-HCV positive people, eight were treated with probably pegylated interferon-based therapy or all oral DAA therapy. Therefore, once diagnosed, the treatment rate seems to be high in South Korea probably because of the high accessibility to health care and relatively low cost of DAA therapy under the coverage of the national health insurance (average out-of-pocket cost of DAA therapy per patient is approximately 2,700 USD, which is 30% of the total cost of DAAs, and 70% of the cost is covered by the national health insurance).

Awareness of HCV infection is one of the important factors to linkage of care. In recent studies, 55.6% of the people in the United States, 36.2% to 66.5% in Taiwan, and 79.5% in Italy were aware of their HCV infection.^{21,27-29} There was only one published study in South Korea, which reported that 34.9% of anti-HCV positive health check examinees were aware of their infection status between 2001 and 2008.³⁰ In previous studies, awareness is usually defined as one's own recognition of HCV infection status, which was verified by anti-HCV results. However, this study did not perform the anti-HCV test for the subjects; therefore, we did not evaluate the verified awareness rate of HCV in South Korea.

This study has several limitations. First, willingness to participate in research could be an inevitable bias in this kind of survey. However, the authors corrected the data through high quality national demographic data and cited the adjusted proportion as the main result of the study. Second, as the anti-HCV testing rate and anti-HCV positive rate are calculated by the respondent's statement, recall bias and possible selection bias may affect the results. Third, only 10 patients were reported as HCV positive; thus, it was difficult to generalize the distribution of age, sex, and area and behavior pattern such as treatment rate and regimen. Finally, knowledge and testing rate of HCV can be influenced by the level of education; this survey did not adjust for the level of education to the national population statistics.

In conclusion, the level of knowledge and testing rate of HCV were relatively low despite the high education level of South Korea. In addition, the majority of the respondents favored the introduction of universal anti-HCV testing through the National Health Examination, especially when people are asymptomatic. To eliminate HCV, publicity and education about HCV are needed, and it is necessary to consider introducing the HCV test to asymptomatic health examinees.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

Study concept and design, data acquisition, analysis, and interpretation, statistical analysis, and manuscript drafting: G.H.C.,

S.H.J. Data acquisition, analysis, and interpretation support: E.S.J., J.W.K. Approval of final manuscript: all authors.

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