

Epidemiology of Hepatitis C Virus in Korea

Hai-Rim Shin

Division of Cancer Control and Epidemiology, National Cancer Center, Goyang, Korea

Key Words

Epidemiology · Genotypes · Hepatitis C virus · Korea · Transfusion

Abstract

Mortality due to liver cancer in Korea ranks as one of the highest in the world. Both hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are high-risk factors for liver cancer. Although HBV is by far the more important risk factor for the development of hepatocellular carcinoma (HCC) in Korea, HCV infection is more closely associated with HCC in elderly patients. Therefore, the evaluation of risk factors for HCV infection, including blood transfusion, is important. This study reviews the literature on HCV prevalence and risk factors among the general population, as well as the distribution of HCV genotypes in Korea. An overall estimate of the prevalence of anti-HCV among Koreans older than 40 years was 1.29% (95% confidence interval 1.12–1.48) during 1995–2000. Blood transfusion was the strongest risk factor for transmission of HCV infection. Risk factors for HCV infection in Korea other than blood transfusion and history of acupuncture have not been proven. The most prevalent HCV genotype is 1b followed by 2a. Even though the prevalence of anti-HCV in Korea has been reduced and the risk of HCV transmission through blood

transfusion has markedly decreased, public-health programs to prevent de novo infections should be developed. Moreover, most people infected with HCV in Korea are older than 40 years, and therefore, the surveillance of adults (≥ 40 years) for HCV infection will be helpful in early detection of HCC developing in them.

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Introduction

As in other countries, infections with both hepatitis B virus (HBV) and hepatitis C virus (HCV) are factors for high risk of developing hepatocellular carcinoma (HCC) in Korea [1]. Of these two, HBV is by far the more important risk factor for HCC in Korea. However, HCV infection is more closely associated with HCC in elderly patients [2]. Since the introduction of screening for anti-HCV of blood donors in Korea in April 1991, the risk of exposure to HCV in blood recipients has remarkably decreased [3]. Therefore, behavioral risk factors rather than blood transfusion influence the epidemiology of HCV infection nowadays. In this study, the literature on HCV prevalence and risk factors among the general population including health examinees in Korea has been reviewed, and the distribution of HCV genotypes in Korea is discussed.

Table 1. The prevalence of anti-HCV among health examinees in Korea during 1995–2000

Study year and area	Subjects n	Anti-HCV	Anti-HCV test method	Study subjects (age group)	Reference
1995–1998 Seoul	86,384	353 (0.41)	radioimmunoassay NANBDINE ¹²⁵ C Kit (General Biologicals Corp., Hsin Chu, Taiwan)	health check-up examinees in a general hospital (≥ 20 years)	Seo WT et al. [9]
1997 Ulsan	10,140	133 (1.31)	3rd EIA, Cobas [®] Core Anti-HCV (Roche Diagnostics, Ind., USA)	examinees for health check-up at University Hospital in Ulsan (≥ 20 years)	Jeong TH et al. [8]
1998–2000 Cheonnam	6,790	142 (2.1)	recombinant HCr43, C200, N55 (Abbott Laboratories, Ill., USA)	examinees for health check-up at Cheonnam University Hospital (≥ 30 years)	Na HY et al. [10]
1997–2001 Daegu	21,291	190 (0.89)	AxSYM (Abbott Laboratories, Ill., USA)	examinees for health check-up at the health promotion center of Dongsan Hospital (≥ 20 years)	Park KS et al. [11]

Figures in parentheses are percentages.

Table 2. The prevalence (%) of anti-HCV among Koreans from four published data during 1995–2000^a

	Prevalence (95% CI)
Age group	
40–49 years	0.57 (0.50–0.66)
50–59 years	1.38 (1.23–1.56)
60 years and older	2.16 (1.86–2.52)
Age-standardized prevalence (≥ 40 years) ^b	1.29 (1.12–1.48)
Estimated number of subjects with anti-HCV	193,000 (168,000–222,000)

^a Data from four publications on health check-ups of middle-aged examinees [8–11].

^b Based on the mean number of population during 1995–2002 and an age-specific estimate of anti-HCV in pooled individuals of 40 years or older.

Seroprevalence of Anti-HCV in Korea

In the 1990s, the overall prevalence of anti-HCV in Korea ranged from 0.7 to 3.5% among middle-aged and older examinees (≥ 40 years) at health check-ups and from 0.4 to 1.5% among healthy individuals with normal levels of alanine aminotransferase [4–9]. During 1995–2000, an overall estimate of HCV prevalence among Koreans older than 40 years was 1.29%, 95% confidence interval (CI) 1.12–1.48; it was estimated on four published data of HCV prevalence in more than 5,000 study subjects (tables 1, 2) [8–11].

Most published data indicate that the prevalence of anti-HCV increases with age. However, few studies examined children and young adults. In Seoul in the year 1995, the prevalence of anti-HCV among children aged 6–11 years was 0.81% (17/2,080) [12] and 0.4% (5/1,350) among young adults of 16–24 years [13]. In Korea, most people infected with HCV are elderly. However, future attention should be paid to the occurrence of de novo HCV infections in age groups other than the elderly.

While some published data show the prevalence of anti-HCV in men similar to that in women, three reports indicate a higher prevalence of anti-HCV in women than in men [6, 14, 15]. The reason for this discrepancy needs to be clarified in future studies.

Risk Factors for HCV Infection

Data published in eight reports unanimously name blood transfusion as the strongest risk of transmission of HCV infection in Korea, with an odds ratio ranging from 1.1 to 25.0 (table 3) [4–8, 14–17]. The average odds ratio of blood transfusion estimated on the eight data sets is 2.64 (95% CI 1.99–3.50). Since less than 1% of the general population receive blood transfusion, the risk attributed to blood transfusion is not very significant among the Korean population today. Comparison of the risk of blood transfusion before and after 1992 has revealed no risk of HCV infection among blood recipients after 1992 [15].

Among the other risk factors reported, histories of surgical operation [14] and acupuncture [15] were significant

Table 3. Odds ratios and 95% CI (in parentheses) of risk factors for HCV infection in nine published data compiled

Risk factors	Seoul 1992 [4]	Seoul 1994 [5]	Seoul 1996 [16]	Pusan 1995 [6]	Three areas 1997 [7]	Ulsan 1997 [8]	Haman 1993 [14]	Haman 1999 [15]	Seoul 1994–1998 [17] (type 1b)	Seoul 1994–1998 [17] (type 2a)
Cases/controls:	72/4,239	36/105	64/128	53/1,753	57/1,624	33/99	63/253	77/623	70/97	63/97
History of hepatitis		NA	3.9 (1.4–10.7) ^a	3.4 (1.5–7.9)		2.1 (NS)				
Family history of liver disease		1.3 (0.5–3.1)			1 (0.3–3.3)	4.4 (NS)				
Blood transfusion										
Yes/no	1.1 (0.5–2.4) ^b	6.7 (2.06–21.9)	2.4 (1.1–5.2) ^a	25.4 (13.8–46.9)	1.5 (0.6–4.1)	6.1 (1.7–22.5) ^a	1.1 (0.2–6.0)	1.8 (0.7–4.4) ^a	3.2 (1.3–7.8) ^a	4.6 (2.0–10.4) ^b
1992 and after								0 (0–1.3)		
Before 1992								5.5 (1.6–19.3)		
Acupuncture history										
Yes/no		0.8 (0.4–1.9)	0.7	NA	NA	0.9 (NS)		1.9 (1.0–3.6) ^a		
1992 and after							1.2 (0.6–2.4) ^c	2.4 (1.2–4.5)		
Before 1992							1.7 (0.7–4.1) ^d	3 (1.4–6.7)		
Repeated								2.1 (1.1–4.0)		
Surgical operation		0.95 (0.4–2.1)	1.8 (NS)	NA	NA	2.3 (0.8–6.7) ^a	2 (1.0–4.1)		1.63 (0.7–3.6) ^a	
Needle sharing		NS	1.8 (NS)		NA				4.08 (0.4–41.2) ^b	
Endoscopy experience					NA	2.1 (0.7–6.5) ^a			2.06 (0.9–4.5) ^a	2.16 (1.0–4.7) ^a
Tattooing		2.7 (0.8–9.3)								

NA = Nonapplicable; NS = nonsignificant.

^a Odds ratio adjusted by multiple logistic regression. ^b Sex adjusted. ^c Less than 10 acupuncture sessions. ^d More than 10 acupuncture sessions.

risk factors among the population in the same rural area. In this area, 34.1% of men and 62.9% of women reported having had acupuncture sessions more than once; the risk of HCV infection attributable to acupuncture was 38.0% (95% CI 8.0–69.5) in total, 9.4% (95% CI 0.5–67.3) in men and 54.5% (95% CI 21.2–87.8) in women [15]. Further studies are needed to survey HCV prevalence and evaluate the role of acupuncture in other populations.

Many studies performed in Western countries have demonstrated that injection drug use is the single most important risk factor for HCV infection [18–21]. In Korea, the use of methamphetamine (Philocon) spread suddenly since the 1980s and became a serious social problem. The overall seropositivity for anti-HCV was 79.2% among 202 drug abusers [22]. The history of injection drug use has not been ascertained in most epidemiologic studies on HCV infection in Korea. According to a study investigating risk factors for HCV infection with reference to HCV genotypes, only 5.0% of the 139 anti-HCV-positive subjects studied during 1994–1998 confided having been sharing needles [17]. Hence, needle sharing was not a significant risk factor for HCV infection in Korea.

Since the incidence of transfusion-associated hepatitis C declined after the introduction of anti-HCV screening of blood donors, the overall prevalence of hepatitis C has

changed in recent years. However, in Korea, the proportion of hepatitis C patients among intravenous drug abusers or individuals with risky sexual behavior is not yet definitively determined.

Intraspousal or intrafamilial infection is suggested as a route of HCV transmission. However, published data in Korea on intrafamilial [23] or intraspousal transmission [14, 15, 24] are very few, with inconsistent results.

Overall, transmission by risk factors other than blood transfusion is very rare. However, subjects at high risk of HCV infection should be monitored, including those with chronic disease related to sexual behaviors. As of now, there are virtually no data on the sexual transmission of HCV infection in Korea.

Distribution of HCV Genotypes in Korea

There have been few data on the distribution of HCV genotypes among the general population in Korea [14, 15, 17]. In a study on the distribution of HCV genotypes among 178 health examinees with anti-HCV and HCV RNA, 1b (39.9%) and 2a (38.2%) were the two most common types, followed by unclassified types (20.2%) and genotype 3 (1.1%) [17]. In another study, 1b was the pre-

Table 4. Distribution of HCV genotypes in nine studies

Reference	Number and subjects with HCV RNA studied	Study year	Method for HCV genotyping	Genotypes			
				1b	2a	others	unclassified
Shin HR et al. [14]	35; general rural population	1993–1995	RT-nested PCR	12 (37.5)	20 (62.5)	type 1a: 2 type 2a+2b: 1	
Kim CJ et al. [30]	75; patients with liver disease	before 1995	PCR for the NS5 region	45 (60.0)	25 (33.0)		5 (7.0)
Lee DS et al. [25]	138; 30 blood donors, 30 HCC patients, 33 chronic hepatitis, 15 liver cirrhosis and 30 hemodialysis patients	before 1996	method of Okamoto and the reverse hybridization method (INNO-LiPA)	98 (71.0)	33 (23.9)	type 2b: 2	2
Ohno O et al. [26]	53; HCV-infected Koreans	before 1996	a new genotyping system based on PCR with genotype-specific core region primers	35 (66.0)	9 (17.0)	type 1a: 1 type 2b: 4 type 1b+2b: 1	3
Han CJ et al. [27]	166; patients with type C chronic liver disease	before 1997	nested RT-PCR with genotype-specific primers	75 (45.2)	85 (51.2)	type 1a: 2 type 2b: 2 type 3a: 2	
Park YS et al. [28]	169; patients with HCV infections	before 1998	PCR-RFLP with four restriction endonucleases (BstUI, HaeIII, NciI, RsaI) on the 5'-untranslated region of HCV	80 (47.3)	72 (42.6)		17 (10.1)
Son HC et al. [29]	29; patients with HCV hepatitis	before 2002	standardized RT-PCR hybridization	15 (51.7)		type 2a+2c: 8 type 2b: 2	4
Kim YS et al. [17]	178; subjects with HCV-PCR in health check-up examinees	1994–1998	RT-PCR	71 (39.9)	68 (38.2)	type 1a: 1 type 3: 2	36
Shin HR et al. [15]	51; subjects with HCV RNA	1999	RT-PCR	21 (41.2)	28 (54.9)	type 1b+2a: 1	1

Figures in parentheses are percentages.

vailing type (71%), followed by 2a (23.9%), 1a (2.1%), 2b (1.5%) and unclassified types (1.5%) among 138 individuals with HCV RNA (30 blood donors, 33 patients with chronic hepatitis, 15 with liver cirrhosis, 30 with HCC and 30 on maintenance hemodialysis) [25]. In the population of the aforementioned rural area where HCV prevails [15], HCV RNA was detected in 66.2% of inhabitants with anti-HCV (51/77). The most prevalent HCV genotype was 2a (54.9% among subjects with HCV RNA), followed by 1b (41.2%), 1b+2a (2.0%) and unclassified types (2.0%). A higher prevalence of HCV genotype 2a in this rural area may be due to frequent acupuncture carried out there. However, the most prevalent HCV genotype among hepatitis patients in Korea was 1b. Estimated on nine data sets, frequencies of HCV genotypes in hepatitis patients were the highest for 1b at 50.6% (95% CI 47.2–53.9), followed by 2a at 38.0% (95% CI 34.8–41.3) (table 4) [6, 14, 15, 17, 25–29].

Discussion

There is no population-based serological study to estimate the prevalence of HCV infection in Korea. A total of 193,000 individuals (95% CI 168,000–222,000) are estimated to be positive for anti-HCV based on the age-specific prevalence compiled from four published data sets by the meta-analysis. There are no data to estimate the role of each route of HCV transmission, although high prevalence of HCV infection among older people may be due to blood transfusion before the 1990s. The risk of HCV exposure among blood recipients has decreased. In Korea, HCV has rarely been transmitted by blood transfusion after the introduction of anti-HCV screening of blood donors, which started in April 1991. The high prevalence of anti-HCV among older people is most likely due to a cohort effect caused by the higher risk of acquiring HCV infection in the distant than in the recent past.

Even though the prevalence of HCV infection in Korea has decreased and the risk of HCV transmission

through blood transfusion has been markedly reduced, public health programs to prevent new infections should be developed. Moreover, in Korea, most people infected

with HCV are older than 40 years, and therefore, the surveillance of HCV infection in adults (≥ 40 years) will help to efficiently detect HCC arising in them.

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