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REVIEW ARTICLE

A review of the burden of hepatitis C virus infection in China, Japan, South Korea and Taiwan

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Abstract Hepatitis C virus (HCV) infection is associated with substantial clinical and economic burden and is an important public health issue in Asia. The objective of this review was to characterize HCV epidemiology and related complications in China, Japan, South Korea and Taiwan. A search of electronic databases and conference abstracts identified 71 potentially relevant articles. Of those, 55 were included in the epidemiology review and 9 in the review of HCV-related complications. HCV prevalence in the general population was 1.6 % in China, 0.6–0.9 % in Japan, 0.6–1.1 % in South Korea and 1.8–5.5 % in Taiwan. Prevalence was higher for injecting drug users (48–90 %) and those with human immunodeficiency virus coinfection (32–85 %) and was lower for blood donors (<1 %). Annual incidence of HCV in China was 6.01 per 100,000. HCV genotype 1b was associated with the highest incidence of hepatocellular carcinoma (HCC). Five-year survival for patients with liver cirrhosis was 73.8 %, decreasing to 39.2 % following liver transplantation; the majority of deaths were attributable to HCC. Limitations were that the majority of studies included in the epidemiology review were small, regional studies conducted in specific populations, and there was an absence of large population-based studies. Thus, estimates may not be representative of the epidemiology of HCV for each country. The prevalence HCV in China and HCV incidence in the Asian region remain largely unknown, and they are likely underestimated. Further epidemiologic and clinical data are needed to provide more precise estimates for use by public health agencies.

Keywords Hepatitis C virus · Epidemiology · Prevalence · Incidence · Genotype · Complications of HCV infection

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Introduction

Globally, HCV infection is a growing public health concern and a leading cause of chronic liver disease and HCC [1]. In Asia, more than 100 million people may be chronically infected with HCV, with about half of those residing in China [2].

A systematic literature review by Sievert et al. [3] published in 2011, estimated that between 49.3 and 64.0 million adults in the Asian region (including India),

Australia and Egypt were anti-HCV positive and that the HCV prevalence in China was greater than in the Americas and Europe combined [3].

Since publication of the Sievert et al. review [3], it has been reported that rates of HCV infection across regions in China are changing, and the genotype distribution is shifting [4, 5].

Accurate estimates of the epidemiologic burden of HCV in the Asian region are critical for health care planning and for understanding unmet clinical needs [6]. This study reviewed the published English-language literature, from 2011, to provide an overview of the current state of the epidemiologic and clinical burden of HCV in China, Japan, South Korea and Taiwan.

Methods

Literature search

The OVID platform was used to search MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) from 2011 (end date of the search reported in the Sievert et al. [3] review) to identify English-language articles that reported the epidemiology of HCV in China, Japan, South Korea and Taiwan. To identify articles that reported comorbidities and complications of HCV in those regions, a search of the same databases, from 2008 to the present, was conducted. Conference abstracts from the Asian Conference on Hepatitis B and C, Human Immunodeficiency Virus (HIV) and Influenza and Viral Hepatitis held in Beijing, China, in 2012 were also searched.

Inclusion/exclusion criteria

To be eligible for inclusion in the epidemiology review, articles had to report the results of observational studies or randomized controlled trials (RCTs), conducted in adults who had laboratory-confirmed HCV (either anti-HCV antibody or detectable HCV RNA). Studies were acceptable if they were conducted in a general population, injecting drug users (IDUs), HIV and HCV coinfected patients, migrants, health care workers, or blood donors and reported the incidence or prevalence of HCV infection. Inclusion criteria for the comorbidity/complication review were similar but required that results be reported as comorbidities or complications of disease or treatment.

Study selection

In a two-step process, studies were assessed against prespecified inclusion/exclusion criteria. In step one, abstracts of articles were assessed and categorized as 'included,' 'unsure' or 'rejected.' In step two, full text articles were obtained for those in the 'included' and 'unsure' categories. The selection process was repeated until all articles were ultimately categorized as 'included' or 'excluded.' Reasons for rejections and exclusions of studies were recorded.

Data extraction

Data were extracted into project-specific Microsoft Excel® tables by one reviewer, and a random 10 % of data extraction was reviewed by a second reviewer. Differences, if any, were resolved by consensus.

Results

Epidemiology review

The literature search identified 836 articles for potential inclusion in the review. Of those, 59 fulfilled all inclusion criteria. An additional four studies were excluded because they had an inappropriate study design ($n = 2$, one letter to the editor and one editorial comment), inappropriate disease ($n = 1$, patient had a diagnosis of paralytic poliomyelitis) and did not report the outcome of interest ($n = 1$, study did not report prevalence or incidence of HCV infection). Thus, 55 articles fulfilled all criteria and were included in the review (Fig. 1).

Of the 55 included articles, 37 were from China, 6 from Japan, 3 from South Korea and 9 from Taiwan. Seven studies were conducted in a general population, and two were conducted in blood donors. All other studies were conducted in specific populations including HIV/HCV coinfected patients, migrant workers, patients on dialysis, IDUs, patients with hematological malignancies and patients with erectile dysfunction.

Prevalence of HCV infection in the general population

Seven studies, two from China [7, 8], two from Japan [9, 10], one from South Korea [11] and two from Taiwan [12, 13], were conducted in a general population. Of those, only two, one from South Korea [11] and one from Taiwan [12], were population-based.

China

The prevalence of HCV infection among the general population in China ranged from 1.6 % in Wuwei City [7] to 28.9 % in Putian County [8] (Table 1).

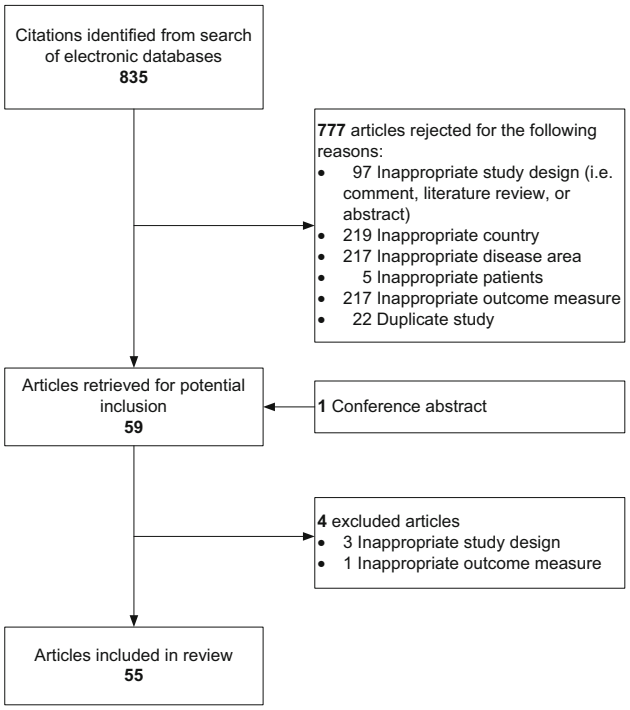

Fig. 1 Flow chart for selection of articles on HCV epidemiology

Participants in the Wuwei study [7], an area of high hepatitis B prevalence, were primarily from rural areas. Of those screened ($n = 7189$), 1.64 % ($n = 118$) were anti-HCV positive when tested by commercial third-generation enzyme-linked immunosorbent assay (ELISA). Of that 118, 37.29 % were detectably HCV-RNA positive as per reverse-transcriptase polymerase chain reaction (RT-PCR), equating to an infection rate of 0.61 % among the general population in Wuwei. According to the authors of that study [7], the distribution of HCV across the four regions of Wuwei differed significantly ($p < 0.01$) with the highest prevalence observed in Liangzhou District (2.49 %) and the lowest in Tianzhu Autonomic County (0.65 %) (Table 1).

In Putian County [8], HCV prevalence was found to increase significantly ($p = 0.0001$) with age, ranging from 12 % in those 20–29 years of age to 69 % in those aged 60–69 years [8]. In fact, more than half of residents over the age of 40 years were infected with HCV. The study authors [8] noted that this finding was unexpected and may have been due to the lack of sterilization of medical equipment that was common practice in this region until the 1990s [8] (Table 1).

Japan

Based on data from a large ($n = 146,857$) study in Ibaraki prefecture, of patients undergoing public health examinations between 2002 and 2007, the prevalence of HCV infection in the general population in Japan was estimated to be 0.9 %. Higher rates were reported for males (1.4 %) than for females (0.7 %) [10] (Table 1).

Estimates of the prevalence of HCV in the general population were also available for working populations in the cities of Ishikawa and Hiroshima (Table 1) [9]. Overall, HCV prevalence was 0.3 % (0.1–0.7 %) in Ishikawa and 0.6 % (0–3.4 %) in Hiroshima. In Ishikawa, HCV prevalence ranged from 0.3 % in those in the 40–49 years of age group to 0.9 % in the ≥70 years of age group. In Hiroshima, the prevalence of HCV was reported only for those in the 50–59 years of age group (1.8 %, range 0–9.9 %). There were five cases of HCV reported among females in Ishikawa (0.5 %) and no reported cases among males. In Hiroshima, there were no reported cases of HCV among females and only one reported case among males (0.6 %) [9] (Table 1).

South Korea

HCV prevalence estimates were available from one study that included 291,314 adults who had received checkups in health centers ($n = 29$) throughout South Korea (Table 1) [11].

The age, sex and area-adjusted anti-HCV positive rate in South Korea was 0.78 % (95 % CI 0.75–0.81). HCV prevalence was significantly ($p = 0.017$) higher among females (0.83 %) than males (0.75 %) after adjustment for age and geographic area. This gender-based difference was seen for all age groups other than those 70 years of age and older. Prevalence increased with increasing age, from 0.34 % for those in the 20–29 years of age group to 2.31 % for the ≥70-year group, and by geographic location, with higher rates observed in coastal areas (1.53–2.07 %) than in Seoul and the city surroundings (0.50–1.20 %) [11] (Table 1).

Taiwan

Based on data from 155 villages in seven townships in Taiwan ($n = 23,820$), the prevalence of HCV infection in Taiwan was estimated to be 5.5 % [13]. The prevalence was higher in older rather than younger participants and varied geographically from 2.0 to 14.2 % for townships on the main island and 2.3–26.4 % in Penghu, an offshore island (Table 1).

The prevalence of HCV infection in Taiwan, based on the control group ($n = 32,145$) of a population-based database study (2000 Registry for Beneficiaries of the Taiwan National Health Insurance program), was estimated to be 1.8 % [12] (Table 1).

Table 1 Summary of results from studies that reported the prevalence of HCV in the general population of China, Japan, South Korea and Taiwan

Author	Study details	Participants	Number in sample	Age group (years)	Prevalence in % (95 % CI)
China, by age group					
Li [7]	Assess HCV epidemiology in Wuwei City, Gansu Province, an HBV-endemic area	NR	7189	All	1.64
			2074	≤20	0.87
			1575	20–40	1.27
			3540	≥40	2.26
Lu [8]	Identify prevalence of both HBV and HCV infections in a village of Putian County, Fujian Province	All villagers in Putian County	1050	Overall	28.9[a]
			110	<10	0.9
			249	10–19	2.8
			92	20–29	12
			233	30–39	34.8[a]
			148	40–49	52.7[a]
			107	50–59	54[a]
			63	60–69	68.8[a]
			48	≥70	0
China, by district					
Li [7]	Assess HCV epidemiology in Wuwei City, Gansu Province, an HBV-endemic area	Liangzhou	3170	All	2.49
		Minqin	1552	All	0.97
		Gulang	1382	All	1.23
		Tianzhu	1085	All	0.65[b]
Japan, by age group					
Katayama [9]	Cross-sectional: general population: Ishikawa	All residents of Ishikawa	1755	All	0.3 (0.1–0.7)
			190	20–29	0
			492	30–39	0
			315	40–49	0.3 (0–1.8)
			270	50–59	0
			364	60–69	0.8 (0.1–2.7)
			224	≥70	0.9 (0.1–3.2)
Katayama [9]	Cross-sectional: workers in Hiroshima	All workers	166	All	0.6 (0–3.4)
			89	20–49	0
			56	50–59	1.8 (0–9.9)
			21	60–69	0
Japan, by gender					
Katayama [9]	Cross-sectional: general population: residents of Ishikawa	Male	784	20–>70	0
		Female	971	20–>70	0.5
Katayama [9]	Cross-sectional: workers in Hiroshima	Male	162	All	0.6
		Female	2		0
Miyazaki [10]	Cohort: annual public health examination: Ibaraki Prefecture	All participants	146,857	All	0.9
		Male			1.4
		Female			0.7
South Korea, by age group					
Kim [11]	Reveal nationwide seroprevalence of HCV infection in South Korea by a large-scale survey at 29 health checkup centers	Health center attendees	8215	20–29	0.26
			70,253	30–39	0.31
			105,245	40–49	0.47
			72,881	50–59	0.65
			26,958	60–69	1.32
			7762	≥70	2.09

Table 1 continued

Author	Study details	Participants	Number in sample	Age group (years)	Prevalence in % (95 % CI)
South Korea, by gender					
Kim [11]	Reveal nationwide seroprevalence of HCV infection in South Korea by a large-scale survey at 29 health checkup centers	Male	178,808	All	0.55
		Female	112,506	All	0.65
South Korea, by district					
Kim [11]	Reveal nationwide seroprevalence of HCV infection in South Korea by a large-scale survey at 29 health checkup centers	Seoul	85,934	All	0.49
		Busan	7856	All	1.76
		Daegu	11,400	All	0.66
		Incheon	11,832	All	0.52
		Gwangju	3505	All	0.77
		Daejeon	5000	All	1.14
		Ulsan	19,105	All	0.56
		Gangwon	9470	All	0.56
		Gyeonggi	92,461	All	0.48
		Chungbuk	4259	All	0.49
		Chungnam	17,027	All	0.42
		Gyeongbuk	5831	All	0.87
		Gyeongnam	3969	All	1.34
		Jeonbuk	7593	All	0.80
		Jeonnam	3647	All	1.86
		Jeju	2425	All	0.25
		Overall	291,314	All	0.59
Taiwan, by age group					
Lee [13]	Case-control study: interviews of villagers from the community	All participants from seven townships	23,820	All	5.5 (5.2–5.8)
			6820	30–39	3.3 (2.9–3.7)
			6240	40–49	4.8 (4.2–5.3)
			7295	50–59	7.3 (6.7–7.9)
			3430	60–65	7.6 (6.7–8.5)
Taiwan, by gender					
Lee [13]	Case-control study: interviews of villagers from the community	Male participants	11,968	All	4.8 (4.4–5.2)
		Female participants	11,817	All	6.2 (5.8–6.7)
Taiwan, by township					
Lee [13]	Case-control study: interviews of villagers from community	Sanchi	1450	All	14.2 (12.4–16.0)
		Potzu	3600	All	7.0 (6.2–7.8)
		Chutung	5402	All	4.1 (3.5–4.6)
		Kaohsu	3874	All	2.0 (1.6–2.4)
		Paihsa	1305	All	26.4 (24.1–28.8)
		Huhsi	1840	All	3.9 (3.0–4.7)
		Makung	6314	All	2.3 (1.9–2.6)
Chung [12]	Case-control study: National Health Insurance database	Population-based controls	32,145[c]	All	1.8

CI confidence interval, *HCV* hepatitis C virus, *HBV* hepatitis B virus, *NR* not reported

[a] Authors reported that the high prevalence in older respondents is due to (historic) inadequate sterilization of medical equipment

[b] Authors reported that there is a significant difference between Tianzhu and Liangzhou ($p < 0.01$)

[c] Control of study (population-based dataset with a case-control design)

Table 2 Incidence of HCV infection in the general population of China, by year

Study design and data source	Geographic region	Subgroup	Year	Annual incidence per 100,000 persons	Cumulative 5-year incidence per 100,000 persons
Case-control study from the China Information System for Disease Control and Prevention in Fujian Province	Province	All	2006	2.63	–
	Province	All	2010	6.01	–
	Province	Male	2006	3.52	–
	Province	Female	2006	1.72	–
	Province	Male	2010	6.80	–
	Province	Female	2010	5.19	–
	Province	Female	2006–2010	–	18.12
	Province	Male	2006–2010	–	26.29
	Province	0–29	2006–2010	–	9.31
	Province	30–59	2006–2010	–	29.93
	Province	>60	2006–2010	–	52.51
	Fuzhou	All	2006–2010	–	29.37
	Xiamen	All	2006–2010	–	29.45
	Putian	All	2006–2010	–	86.95
	Sanming	All	2006–2010	–	16.07
	Quanzhou	All	2006–2010	–	12.03
	Zhangzhou	All	2006–2010	–	5.54
	Nanping	All	2006–2010	–	8.82
	Longyan	All	2006–2010	–	12.96
	Ningde	All	2006–2010	–	18.09

Source: Study of Wu et al. [14]

A dash indicates "not applicable." Definition of a new case was the seroconversion from HCV antibody negative at initial testing to HCV antibody-positive during the study

HCV hepatitis C virus

Incidence of HCV infection in the general population

One study from China [14] provided data on the incidence of HCV infection among the general population. There were no studies identified that reported the incidence of HCV infection among the general population in Japan, South Korea or Taiwan.

China

The annual incidence of HCV infection among the general population in Fujian Province increased from 2.63 % (95 % CI, 2.46–2.79 %) in 2006 to 6.01 % (95 % CI, 5.76–6.26 %) in 2010 [14]. In 2006, the incidence of HCV infection in males (3.5 per 100,000 persons) was substantially higher than in females (1.72 per 100,000 persons). By 2010, the difference in prevalence of HCV infection between males (6.80 per 100,000 persons) and females (5.19 per 100,000 persons) had narrowed (Table 2).

The cumulative 5-year incidence of HCV infection in Fujian Province varied considerably by region, with substantially higher rates in Putian (86.95 per 100,000 persons) than all other regions (range 5.4–29.45 per 100,000) (Table 2; Fig. 2).

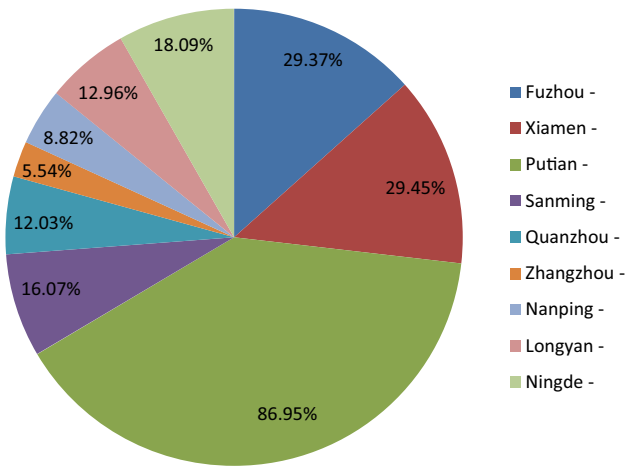

Fig. 2 Incidence of HCV infection in the general population of China, 2006–2010, by province

Prevalence of HCV infection in blood donors

Two studies, one from China [15] and one from Japan [16], provided data on the prevalence of HCV infection among blood donors. There were no studies identified that reported the prevalence of HCV among blood donors in South Korea or Taiwan.

China

In China, the HCV prevalence among commercial blood donors ($n = 3062$) was 12.7 %, ranging from 9.7 % in blood donors who were HBV positive to 85 % among those who were HIV positive (Table 3) [15].

Japan

In Japan, the prevalence of HCV among first-time volunteer blood donors ranged from 0.065 to 0.300 % (Table 3).

Prevalence of HCV infection in high-risk populations

Nineteen studies reported the prevalence of HCV infection in high-risk populations: ten were from China [17–26], two from Japan [27, 28], two from Korea [29, 30] and five from Taiwan [12, 31–34].

Among high-risk populations, the prevalence of HCV infection was higher among IDUs (48–95 % in China,

Table 3 Summary of results from studies that reported the prevalence of HCV in commercial or volunteer blood donors in China, Japan, South Korea and Taiwan

Author	Study details	Participants	Number in sample	Age group (years)	Prevalence in % (95 % CI)
China					
Dong [15]	Shanxi Province: HIV-endemic area	All commercial donors	3062	NR	12.7
		HIV-positive donors	40		85
		HBV-positive donors	103		9.7
Japan					
Tanaka [16]	Nationwide retrospective study: 8 jurisdictions of the Japanese Red Cross Blood Center	First time volunteer blood donors	1,205,966	20–24	0.065 (0.061–0.070)
			536,560	25–29	0.114 (0.105–0.123)
			408,814	30–34	0.186 (0.173–0.200)
			278,024	35–39	0.300 (0.279–0.320)
		Attendees at periodical health checkups for HCV screening	611,146	40–44	0.348 (0.333–0.363)
			495,032	45–49	0.463 (0.444–0.482)
			675,350	50–54	0.516 (0.499–0.533)
			947,438	55–59	0.631 (0.615–0.646)
			1,081,854	60–64	0.779 (0.762–0.795)
			1,264,496	65–69	1.085 (1.067–1.103)
			1,054,472	70–74	1.674 (1.649–1.698)
Tanaka [16]	Simulated estimation of undiagnosed HCV carriers: 8 jurisdictions of the Japanese Red Cross Blood Center Entire Nation	Hokkaido	5,620,813	NR	0.46
		Tohoku	12,047,975		0.40
		Kanto	41,247,892		0.57
		Hokuriku/Tokai	19,294,443		0.69
		Kinki	22,657,542		0.52
		Chugoku	7,650,977		0.70
		Shikoku	4,083,698		0.86
		Kyushu	14,682,313		0.80
		Japan	127,285,653		0.63
South Korea					
	No studies identified				
Taiwan					
	No studies identified				

CI confidence interval, *HCV* hepatitis C virus, *HBV* hepatitis B virus, *HIV* human immunodeficiency virus, *NR* not reported

South Korea and Taiwan) [19, 20, 32] than individuals undergoing hemodialysis (6.6 % in China) [17] and those with HIV/HCV coinfection (32–68 % in China) [24, 25] (Table 4).

The prevalence of HCV among migrant workers in Zhejiang, China, was 0.4 % [26] and 1.6–2.1 % for those in Japan. Higher prevalence was observed among migrant workers in Japan who originated form Northeast China than from other regions of China [27] (Table 4).

Prevalence of HCV, by genotype

Five studies, four [7, 35–37] from China and one [38] from Taiwan, reported the prevalence of HCV by HCV genotype. No studies were identified that reported the prevalence of HCV by HCV genotype in Japan and South Korea.

In China, the most commonly observed HCV genotype among the general population [35], and among those attending hepatitis clinics [36, 37], was genotype 1b (Table 5; Fig. 3). For persons living in HBV-endemic areas, the most commonly observed HCV genotype was genotype 2a [7] (Table 5).

In Taiwan, genotype 1b was found to be the most prevalent genotype (54.8 %) [38] (Table 5).

Comorbidities/complications review

The literature search identified 142 articles for potential inclusion in the review. Of those, 134 were excluded because of an inappropriate study design ($n = 35$), inappropriate disease ($n = 67$), inappropriate patient population ($n = 5$), inappropriate intervention ($n = 1$), inappropriate outcome measure ($n = 10$) and inappropriate country ($n = 16$). One conference abstract, two articles identified from the "epidemiology" literature search and one article obtained from the authors were included to yield 12 articles for potential inclusion; a further 3 were excluded because of an inappropriate country, outcome measure (all patients had compensated liver cirrhosis and complications were not reported) and disease (patients had a diagnosis of diabetes). Thus, a total of nine articles provided information on comorbidities and complications of HCV (Fig. 4).

Of the nine included articles, there were three from China and two each from Japan, South Korea and Taiwan. The objectives of the nine studies varied greatly and included examination of HCV-related complications by HCV genotype, survival of liver transplant recipients with HCV-related HCC, liver fibrosis by status of HIV/HCV coinfection, liver disease progression, metabolic syndrome and long-term risk of HCC.

Complications of HCV infection included liver cirrhosis, ascites, esophageal varices, hepatic encephalopathy, HCC (5–13 %) and death (5-year survival was 73.8 %) [39]. Retinopathy was identified as a complication of pegylated interferon and ribavirin combination therapy [40]. High body mass index, hypertension and insulin resistance were common features of individuals with HCV [41]. Furthermore, HIV/HCV coinfected individuals had worse fibrosis scores than monoinfected individuals [36, 37]. Relatively young HIV/HCV coinfected individuals had advanced liver disease (ascites, hepatic encephalopathy or HCC) [42].

Of all HCV genotypes, genotype 1b was associated with the highest incidence of HCC [35, 43] and the highest prevalence of compensated cirrhosis (5.7 %), hyperlipidemia (6.4 %), ascites (3.1 %) and portal hypertension (2.7 %) [35]. HCV genotype 3 had the highest prevalence of decompensated cirrhosis (6.6 %), fatty liver history (15.4 %) and insulin resistance (4.4 %) of all genotypes [35]. For those with chronic HCV infection, the overall tumor-free, hepatitis-free 5-year survival rate following liver transplantation was 39.2 % [44]. The 1-, 3- and 5-year overall survival rates after liver transplantation were significantly worse in HCV-HCC patients than in HBV-HCC patients (64.6, 42.8 and 39.2 % in HCV patients vs. 76.7, 56.6 and 49.1 % in HBV patients, $p < 0.001$) [44]. Finally, individuals coinfected with HIV and HCV had worse liver fibrosis and advanced liver disease at an earlier age relative to monoinfected individuals [36].

Discussion

In this study, HCV prevalence varied substantially across the Asian region, with higher rates reported in Taiwan (1.8–5.5 %) than in China (1.6 %), South Korea (0.6–1.1 %) and Japan (0.6–0.9 %). These findings are consistent with those reported by Sievert et al. [3] for Taiwan 4.4 %, China 1–1.9 % and Japan 1–1.9 % and by Hanafiah et al. [2] (Taiwan 3.7 %, China 3.7 % and Japan 1.4 %) [2].

For South Korea, the overall prevalence estimate in the current review (0.6–1.1 %) is slightly lower than those reported by Sievert et al. [3] (1.3–1.4 %) and by Hanafiah et al. (1.4 %) [2]. This difference may be due to inclusion of a nationwide survey by Kim et al. [11] in the current review that was unavailable at the time of the reviews by Sievert et al. [3] and Hanafiah et al. [2]. The Kim et al. [11] survey included a high proportion of young and middle-aged workers (89 % were <59 years of age) living in urban areas. However, as the HCV infection rate in South Korea is typically higher in older individuals (>60 years of age) and in those living in rural areas than in the younger urban-dwelling population, the inclusion of the overall estimate from the Kim et al.'s [11] paper may have underestimated the HCV prevalence.

Table 4 Summary of results from studies that reported the prevalence of HCV among high-risk populations in China, Japan, South Korea and Taiwan

Author	Year/s of analysis	Study design/data source	Number in sample	Age group (years)	Prevalence (%) of HCV (95 % CI)
China					
Hemodialysis patients					
Yuan [17]	2007	Zhejiang Province: maintenance hemodialysis patients	6182	NR	6.6
Females who have sex with females					
Wang [18]	NR	Adults	216	NR	0.5
Injecting drug users					
Fu [19]	2010	Shanwei City, Guangdong mandatory detoxification center	210	NR	71.4
			198		94.5
Wu [20]	2009	Zhenjiang Methadone Treatment Center, Jiangsu Female's re-education through labor camps	141	NR	81.6
Injecting drug users attending methadone programs					
Du [21]	2008	Shanghai	114	NR	57
Wang [22]	NR	Changsha and Wuhan	294	NR	82.3
Hser [23]	2009–2010	Shangai and Kunming	306	NR	53.3
		Kunming	146		55.5
		Shangai	160		51.3
HIV-positive patients					
He [24]	2008–2009	HIV-positive patients attending local CDC for routine follow-up of positive CD4 cell count	1110	All	59.0
			191	18–29	37.5
			503	30–39	62.2
			290	40–49	66.3
			96	50–59	67.7
			30	60–94	43.3
Yan [25]	2007–2008	Male: negative for HbsAg	3241	NR	45.3
		Male: positive for HBsAg			42.2
		Female: negative for HBsAg	1065		31.8
		Female: positive for HBsAg			34.7
Migrant workers					
Pan [26]	2010	Overall	17,377		0.4 (0.31–0.51)
		History of casual sex	12,694		1.8
		Males engaged in commercial sex	NR		1.3
Japan					
Chinese immigrants, by area of origin					
Yan [27]	2010–2011	North Chinese	32		0
		Central Chinese	9		0
		South Chinese	1		0
		East Chinese	180		1.67
		Northeast Chinese	327		2.14
		Southwest Chinese	10		0
		Hong Kong, Taiwanese	5		0
Individuals with oral lichen planus					
Nagao [28]	2010–2011	Checkup for oral mucosal diseases at Kurume University Hospital	59		59.32
South Korea					
Intravenous drug users					
Min [29]	NR		318	NR	47.5–48.4

Table 4 continued

Author	Year/s of analysis	Study design/data source	Number in sample	Age group (years)	Prevalence (%) of HCV (95 % CI)
Hematological malignancies					
Kang [30]	NR	Cases	3932	52.8	2.4
Taiwan					
Males who have sex with males (MSM)					
Tseng [31]	2010	MSM	1123	18–40	2.4
		MSM who are HIV positive	434		5.5
Intravenous drug users					
Liao [32]	2004–2005		274	21–66	78.1
Institutionalized individuals					
Hung [33]	2000	Males	346	20–70	2.6
		Females	242	20–70	0.8
		All	588	20–70	1.9
Hung [33]	2000	All, by age group	34	20–29	2.9
			184	30–39	2.2
			203	40–49	1.5
			126	50–59	0.8
			33	60–69	3.0
			8	≥70	12.5
Splenic lymphoma patients					
Yu [34]	1988–2011	Positive for anti-HCV	41		27
		Positive for HCV viral RNA	41		12
Patients with erectile dysfunction					
Chung [12]	2001–2009	Cases of ED	6429		2.8

CD4 cluster of differentiation four, *CDC* Center for Disease Control, *CI* confidence interval, *ED* erectile dysfunction, *HBsAg* hepatitis B surface antigen, *HCV* hepatitis C virus, *HBV* hepatitis B virus, *HIV* human immunodeficiency virus, *MSM* males who have sex with males, *NR* not reported, *RNA* ribonucleic acid

Table 5 Prevalence of HCV genotypes in the general population of China, Japan, South Korea and Taiwan

Study design and data source	Genotype (%)							Reference
	1a	1b	2a	2b	3a	3b	6a	
China								
Questionnaire: HBV-endemic area		34.1	59.1					Li et al. [7]
Nationwide cross-sectional hospital survey	1.4	56.8	15.2	0.2	3.5	5.2	5.7	Rao et al. [35]
Retrospective cross-sectional study in hepatitis clinics	3.1	64.3	7.1		3.1	7.1	15.3	Wang et al. [36, 37]
Japan	No studies identified							
South Korea	No studies identified							
Taiwan								
Community-based interviews in villages	5.7	54.8	28.5	11.0				Lee et al. [38]

HCV hepatitis C virus, *HBV* hepatitis B virus

Not only did prevalence estimates differ across countries, they differed within countries. Most estimates, however, were based on small regional studies or on special patient populations, which likely contributed to the large variability in rates within each country and perhaps across countries as well. Large, population-based, surveillance and reporting programs are necessary to enable the collection of high-quality, robust data on the epidemiology of HCV infection in the Asian region.

Despite the differences in prevalence across North Asia, there were similarities in the prevalence distribution across countries. First, compared to the general population, the

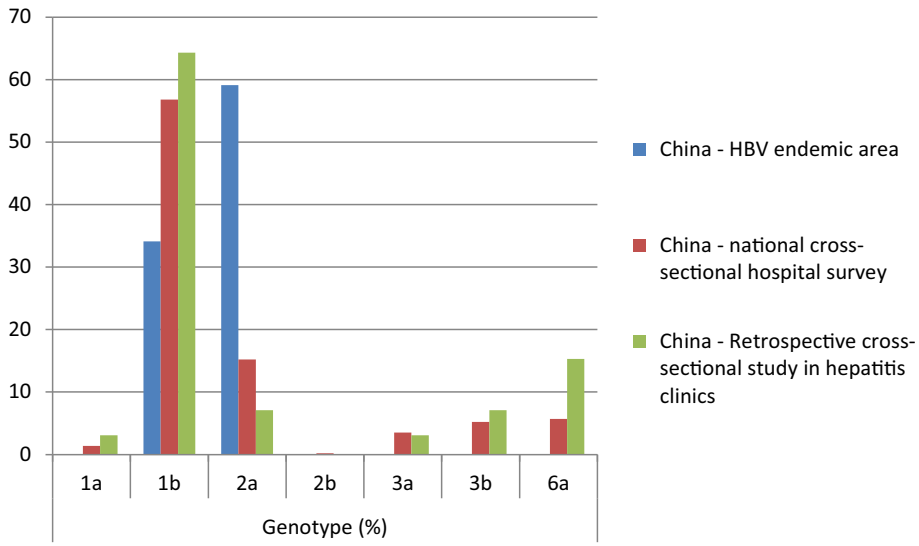

Fig. 3 Distribution of HCV genotypes in China, by source of data

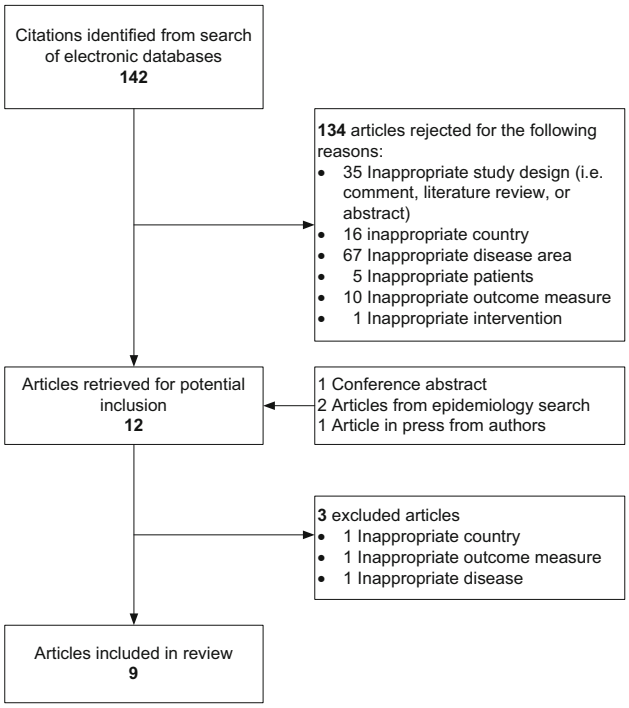

Fig. 4 Flow chart for the selection of articles on comorbidities/complications

prevalence was substantially higher among IDUs (48–95 % in China, South Korea and Taiwan), individuals undergoing hemodialysis (6.6 % in China) and those with HIV/HCV coinfection (32–68 % in China). A recent analysis of two national databases, i.e., the China's national medical HCV case report system and the national disease sentinel surveillance system, indicated a compelling transmission of HCV in drugs users and persons undergoing invasive medical treatment, particularly hemodialysis [45]. In order to improve care for vulnerable groups with HCV infection, the World Health Organization (WHO) has recently released guidelines that include recommendations for the screening, care and treatment of HCV infection for special populations, including the promotion of human rights, equity and antidiscrimination laws, and improvement in access to medical and social services [46].

Second, HCV prevalence in all countries examined increased with advancing age, and HCV genotypes 1b and 2 were the most common genotypes among the general populations, although no recent data (2011–2014) were available for Japan or South Korea. A cohort study from Taiwan that examined the association of HCV genotypes and the risk for HCC found that HCV 1b was an independent risk factor for HCC and that genotype 1b carried a higher risk for HCC than genotype 1a [38]. In addition, it was estimated that the cumulative lifetime risk for HCC is 6.5, 19.2 and 29.7 % for those with HCV RNA levels <1000 IU/ml, HCV non-1b and HCV 1b, respectively ($p < 0.001$) [38, 47]. The predominance of genotype 1b among the general population in Asia and the elevated risk of developing HCC for patients with HCV genotype 1b represent a significant public health burden. This fact implies that treatment of HCV should be tailored to the HCV subtype, especially in the era of direct-acting antivirals (DAAs).

For drug users and immune-compromised patients, HCV genotype distribution varied from country to country. Genotype 6a was the most often reported HCV genotype among IDUs and patients with HIV/HCV coinfection in China, while genotype 2a was predominant among IDUs in Taiwan.

HCV-associated complications are numerous, including liver cirrhosis, ascites, esophageal varices, hepatic encephalopathy, HCC and death [39]. Of concern, HCV genotype 1b, the most commonly occurring genotype in

China and Taiwan, is associated with a higher risk of HCC [35, 43], compensated cirrhosis, hyperlipidemia, ascites and portal hypertension [35] than other HCV genotypes. It has been noted that consideration should be given to customizing the management of patients with HCV by viral subtype [38].

For those with chronic HCV infection who undergo liver transplantation, the overall tumor-free, hepatitis-free 5-year survival rate is 39.2 %, with lower rates for those with HCV/HCC than for those with HBV/HCC [44]. For patients with HIV/HCV coinfection, advanced liver disease occurs at an earlier age than for monoinfected individuals [36].

There are a number of limitations to this study. First, as noted above, the original studies that provided prevalence and incidence estimates were small regional studies or included specific patient populations rather than the general population. There were no population-based studies for China and Japan and only one each for Taiwan and South Korea. Furthermore, the general population-based study from South Korea included predominately younger participants (mostly younger than 60 years), which may have led to underestimating the prevalence. The absence of large population-based studies may have contributed to the variability in rates within and across countries. Thus, the estimates reported here may not be representative of the prevalence of HCV for each country.

Second, it has been reported that as many as 35 % of patients may be unaware of their HCV infection status [48]. If this is the case, the prevalence rate reported in the single survey-based study for South Korea may underestimate the true prevalence for that country.

Conclusions

The epidemiologic and clinical burden of HCV in Asia is substantial. In China alone, there are an estimated 20 million cases of HCV, of which 10 million are due to HCV genotype 1b. Nevertheless, uncertainty about the prevalence of HCV infection remains, particularly in China. Furthermore, it is likely that estimates of the prevalence of HCV in Asia are understated because of the general lack of disease awareness in that region and a lack of national surveillance programs.

Despite the increasing importance of HCV as a public health concern in Asia, good-quality epidemiological data are still lacking, and the incidence of HCV in Asia remains largely unquantified. There is a paucity of data in the published literature on the epidemiology of HCV in the Asian region. This is particularly the case for data on the incidence of this infection. As noted by the WHO [46], many of those infected with HCV, in both the general and high-risk populations, remain untested and undiagnosed. Additional data on the epidemiology of this disease are needed to provide more accurate estimates for use by public health agencies. National surveillance systems and screening programs are needed to address the gaps in our knowledge on the epidemiology of HCV in this region.

The burden of HCV infection in Asia indeed necessitates more attention from healthcare policy makers in terms of education and resource allocation.

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