

## Regional Distribution of Hepatitis C Virus Infection in the Republic of Korea, 2007-2011

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**Background/Aims:** In Korea, hepatitis C is included as an infectious disease in a sentinel surveillance system. Recently, a large variation in hepatitis C incidence between different regions in Korea has been noticed. The current study verified the nationwide distribution of hepatitis C infection for effective prevention and management. **Methods:** We counted the number of hepatitis C patients who visited a hospital per county using the National Health Insurance database from 2007 to 2011. The age-adjusted prevalence ratio was used, and the age adjustment method was used as an indirect standardization method. Disease mapping and spatial analysis were conducted using a geographic information system. **Results:** The annual prevalence of diagnosed hepatitis C was approximately 0.12% to 0.13% in Korea. The age-adjusted prevalence ratios in Busan, Jeonnam, and Gyeongnam were high (1.75, 1.4, and 1.3, respectively). The three regions in the southern coastal area of the Korean Peninsula were identified as a high-prevalence cluster (Moran's index, 0.3636). **Conclusions:** The present study showed that hepatitis C infection has very large regional variation, and there are several high-risk areas. Preventive measures focusing on these areas should be applied to block the transmission of hepatitis C and reduce the disease burden. (*Gut Liver* 2014;8:428-432)

**Key Words:** Hepatitis C; Infection; Prevalence; Republic of Korea; Spatial analysis

### INTRODUCTION

Hepatitis C is the infected status of the hepatitis C virus (HCV) which is a positive strand RNA virus. Existence of HCV became known for the first time in 1989 and it is a global public health concern due to its high potential to chronic disease and continued high prevalence.<sup>1</sup> Active prevention is necessary because hepatitis C creates a chronic infection in 85% of infected patients, 10% to 20% and 1% to 5% in the liver cirrhosis and developing liver cancer.<sup>2</sup> According to the World Health Organization statistics, of the world's approximately 123 million people affected by chronic hepatitis C, the prevalence is estimated to be about 2%.<sup>3</sup> Hepatitis C is widely distributed in the world today. Some areas of Africa and the Middle East are known for high prevalence.<sup>4</sup>

In Korea, a large number of hepatitis C patients have been reported. Hepatitis C has been designated as a notifiable infectious diseases with sentinel surveillance system from 2000 in Korea.<sup>4</sup> The major mode of transmission for hepatitis C is blood transfusion and invasive medical practice, which is similar with hepatitis B. Rarely, maternal blood spread through vertical transmission is also possible.<sup>5</sup> Transfusion transmitted infections in Korea seem to be greatly reduced after the blood donor test for hepatitis C was conducted in 1991. However dialysis, intravenous drug abuse, unhygienic acupuncture, sexual contact, and tattoo may also be the risk factors of HCV infection.<sup>6</sup> Risk factors of HCV infection can be distributed differently among the region or population group. Therefore, systematic investigations about regional distribution of hepatitis C and related factors are needed for controlling the disease.

The prevalence of hepatitis C makes a big difference by region as well as by country.<sup>7</sup> Regional differences occur because the environment and cultures, associated with HCV infection

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of each region are different.<sup>8</sup> Egypt has known for the highest prevalence of hepatitis C in the world. Higher prevalence was observed in the river basin regions where the invasive schistosomiasis treatment was widely used.<sup>9</sup> Until now, however, there is no study concerning regional distribution of hepatitis C in Korea.

Therefore, purpose of the current study is verifying Korea's nationwide distribution of hepatitis C for effective prevention and management. At the same time, the present study will be the basis for in-depth epidemiological investigation in high risk regions.

## MATERIALS AND METHODS

### 1. Analysis data

In this study, the National Health Insurance data was used to study the 'prevalence of diagnosed hepatitis C' in each region. The National Health Insurance data we used was regional data based on the patient's address. Therefore, if a patient visited multiple hospitals reside in different regions, the patient's address was considered as the patient's region. Prevalence of diagnosed hepatitis C was calculated as hepatitis C patients who diagnosed in healthcare institutions. These include the patients who cared at institutions, discovered by health screening or diagnosed incidentally, such as routine preoperative evaluation. The number of patients between January 2007 and October 2011 with chronic hepatitis C diagnostic code (B18.2 of International Code of Diseases 10th version) for each region was used. Regional divisions were large regions (province) and small regions (county) based on administrative boundaries. If a patient received treatment several times in the same year, the count was adjusted to 1 person to avoid duplication.

### 2. Age adjustment

The age-adjusted prevalence ratio (APR) was used because the prevalence of hepatitis C increases with age. Indirect standardization was used to compare the prevalence among regions because each regional age-specific patient number was very small. Standard rate for calculating APR was this data's national age-specific rate and the denominator population was from the 2010 Census population. Used software for age standardization was Microsoft Excel 2007 (Microsoft Corp., Redmond, WA, USA) program. After comparisons among all provinces, comparisons among counties belong to three high APR provinces were done.

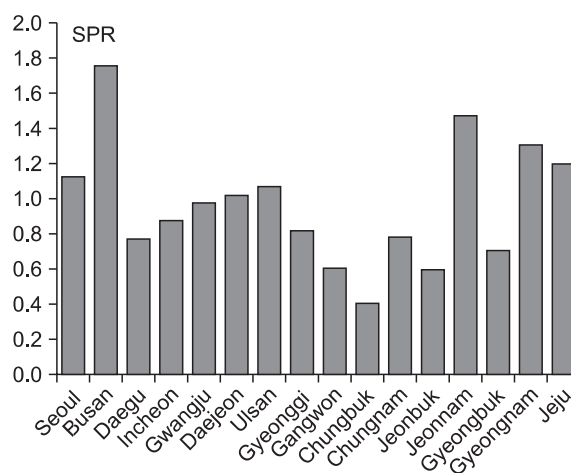
## 3. Spatial analysis

The grid map was drawn according to the administrative district boundaries divided into five levels to make it easy to see the difference between regions. Spatial autocorrelation analysis was performed using Moran's index to see whether the prevalence is spatially biased or not. Moran's index has the range from -1 to 1 and it is most popular spatial autocorrelation measuring index. Spatial autocorrelation means that risk distribution is related to the spatial location thus if the Moran's index become close to 1 or -1, it means strong autocorrelation.<sup>10</sup> If the Moran's index is 1, risk distribution is fully clustered but -1 means fully dispersed distribution. Additionally, local indicators of spatial association (LISA) analysis was conducted to find the regional cluster of statistically significant ( $p < 0.05$ ) higher and lower clusters.<sup>11</sup> The software program for spatial analysis was OpenGeoDa (ver.0.9.9.11). Actual province names were used, but county names were anonymized to avoid the premature stigma.

## RESULTS

### 1. Annual number of hepatitis C patients and prevalence

Approximately 60,000 patients per year were diagnosed hepatitis C and did not show a clear trend of increase or decrease in 2007 to 2011. In average of this duration, the crude prevalence



**Fig. 1.** Average age-adjusted prevalence ratio of hepatitis C by province in Korea, 2007-2011.

SPR, standardized prevalence ratio.

**Table 1.** Number of Patients and Prevalence of Diagnosed Hepatitis C by Year in Korea, 2007-2011

	2007	2008	2009	2010	2011 (to Oct)
No. of patients	64,877	59,704	61,901	61,909	59,188
Prevalence of diagnosed hepatitis C, %	0.1317	0.1205	0.1244	0.1226	0.1167*

\*Prevalence of 2011 year was calculated by 10-month data.

of diagnosed hepatitis C was approximately 0.12% to 0.13% (Table 1).

**2. Comparison of province prevalence**

Province prevalence variation was high. Busan showed the highest APR, 1.76 subsequently, Jeonnam 1.48, Gyeongnam 1.31, Jeju 1.20, and Seoul 1.13 in order. Chungbuk region was shown to have the lowest APR was 0.42 (Fig. 1).

**3. Comparison of county prevalence**

The APR for all counties belonging to Busan was more than 1 higher than the national average. Among them, K and O regions appeared unusually high, respectively at 3.95 and 2.96 (Fig. 2). Small region APR variation of Jeonnam was very high. Regions with over the 3 and under the 0.5 were appeared together. There are unusually high regions were S, L, and H showed 3.46, 3.44, and 2.88, respectively (Fig. 2). Small region APR variation of Gyeongnam was very high also. Regions with over the 3.5 and under the 0.5 appeared together. There are unusually high regions where E, P, and H showed 3.95, 2.69, and 2.51, respectively (Fig. 2).

**4. Analysis of the national map**

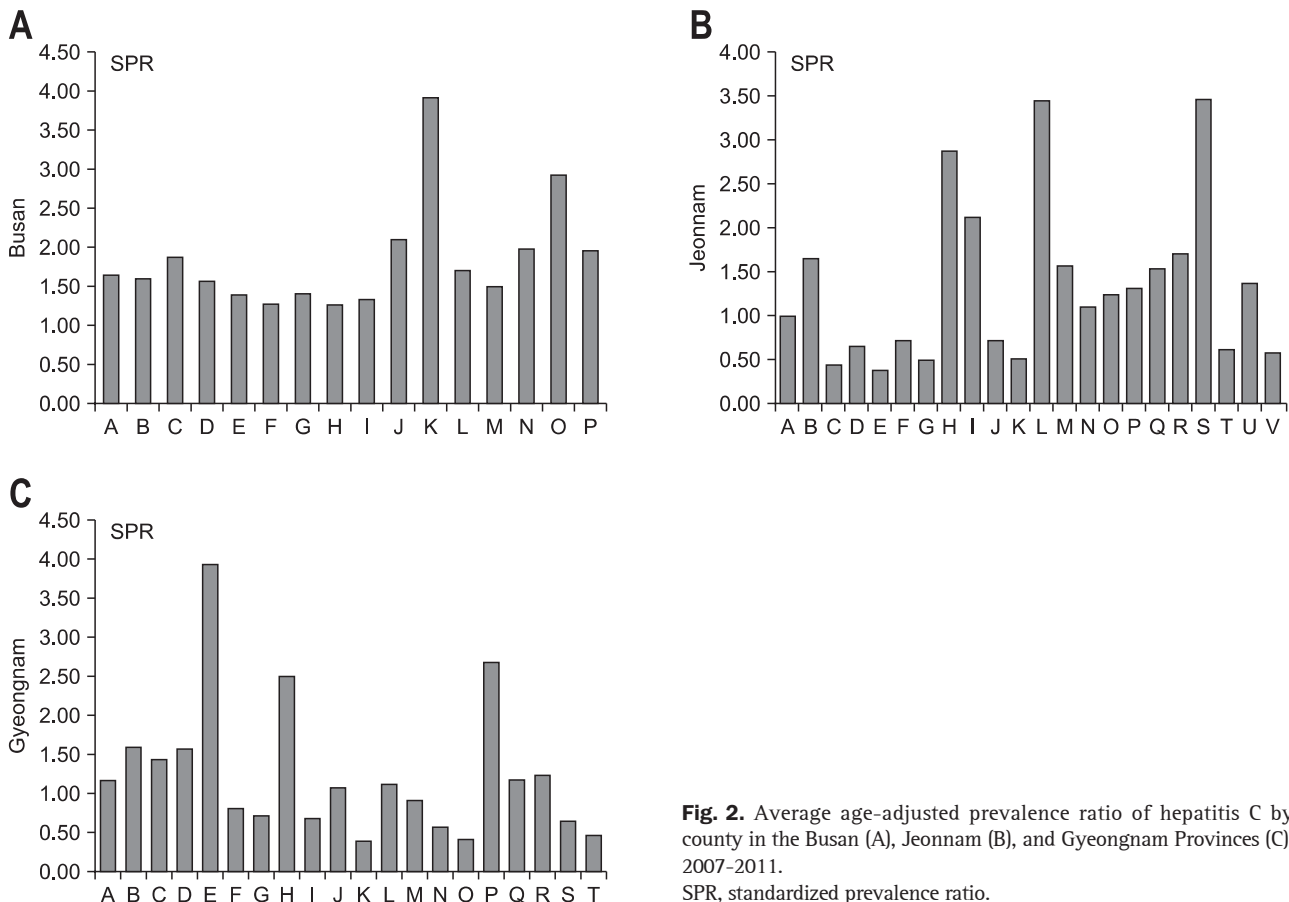
According to the national map drawn by prevalence level of

small regional units, southwest coast and south coast regions have generally shown a high prevalence (Fig. 3). Spatial auto-correlation was significant (Moran's index, 0.3636;  $p < 0.05$ ). At LISA analysis, inland regions of Gangwon, Gyeongbuk, and Chungbuk showed broad cold spots, which means they appear on the low prevalence cluster. High APR regions belonging to Busan, Jeonnam, and Gyeongnam showed three hot spots which means they appear on the high prevalence cluster (Fig. 4).

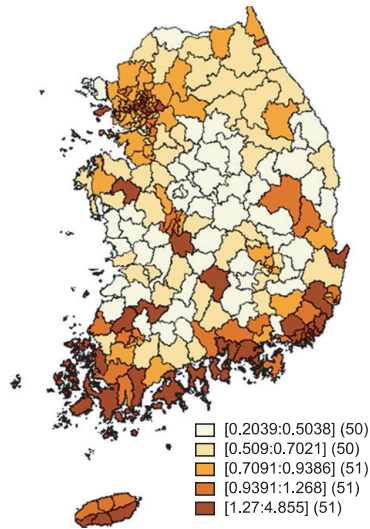
**DISCUSSION**

There are few national data on hepatitis C in Korea because hepatitis C is designated not as a national notification surveillance system but a sentinel surveillance system. In addition, HCV antibody tests were conducted at a few health care institutions or a few regional communities thus meaningful regional comparison could not be conducted. However, Korea has implemented the entire National Health Insurance billing thus the diagnostic code for hepatitis C is given to all patients who visit medical facilities. Therefore the National Health Insurance data can be the most reliable data for studying hepatitis C in Korea. Hepatitis C is confirmed by a laboratory diagnosis, so the variation of medical doctor's disease diagnosis is relatively small.

Prevalence of diagnosed hepatitis C in Korea was calculated



**Fig. 2.** Average age-adjusted prevalence ratio of hepatitis C by county in the Busan (A), Jeonnam (B), and Gyeongnam Provinces (C), 2007-2011. SPR, standardized prevalence ratio.



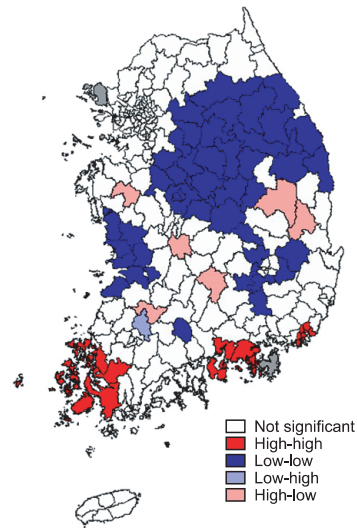
**Fig. 3.** Grid map for each regional average age-adjusted prevalence ratio (APR) for diagnosed hepatitis C, 2007-2011. The colors were divided into five classes, and a high prevalence is indicated by dark brown. The color of each class, range of regional APR, and number of counties belonging to the class are shown.

and regional comparisons were performed using health insurance data during last 5 years. The prevalence of hepatitis C, at 40 years of age or older, in Korea was known to be 1.68% (95% confidence interval, 1.51 to 1.86) in the previous study.<sup>12</sup> In our study, the prevalence of diagnosed hepatitis C was calculated as 0.12% to 0.13% and is much lower than known prevalence. This is due to hepatitis C being usually asymptomatic and the patients often does not visit the hospital or does not care even if he get diagnosed.<sup>13</sup>

When compared by province unit, variation of prevalence was very large and regional difference was greater than the annual difference. In a previous study with adults underwent health check-up, the high prevalence of Busan and Jeonnam have been measured also.<sup>14</sup> Therefore, the control measures for the hepatitis C should be different from region to region.

More detailed analysis of three high APR provinces, two counties in Busan, three counties in Jeonnam, and three counties in Gyeongnam showed high APR. They have a commonality of location on the coast and they are adjacent to each other. The regions are not only geographically bordering but also share local culture and characteristics. For this reason, residents of the regions are likely to have been exposed together with risk factors of hepatitis C. Therefore, a social liberal arts approach to the problem seems to be necessary. Higher hepatitis C prevalence of coastal residents was reported in Japan.<sup>15</sup> This study reported that some villages located on the southwest coast showed high prevalence of hepatitis C.

Busan's highest APR counties have the same feature that the harbor is located in there. There are many human and material moving at these regions. In general, there are more frequent contacts with foreigners in these regions. Hence the behavior



**Fig. 4.** Cluster map of each regional average age-adjusted prevalence ratio for diagnosed hepatitis C, 2007-2011. The spatially nonsignificant regions were marked in light grey. The hot spots were marked in red, which means the prevalence in the region and in neighboring regions was high. The cold spots were marked with blue, which means the prevalence in the region and in neighboring regions was low. Sky blue indicates that the prevalence in the region was low but that in neighboring regions was high. Pink indicates that the prevalence of the region was high but that in neighboring regions was low.

study of harbor workers and blood tests is needed.

Jeonnam's three counties with the highest APR are adjacent to each other on the west coast of Korea and mainly consist of the island. Elderly population proportion of Jeonnam is high but the age-adjusted outcome was used for in this study. It is interesting that only this region's prevalence was high but Jeonnam's south coast regions were not. Due to these region's geographical characteristics, they are likely to have their own culture and health behavior similar to each other. As a result of this study, it is difficult to estimate the risk factors of high prevalence so additional field epidemiological investigations will be required.

Gyeongnam showed high prevalence of three adjacent counties, it seems to have the same locality and the region's residents are likely to have been exposed to certain risk factors together. From the interviews of health center officials in this region, invasive "Buhwang" therapy and unlicensed phlebotomy is highly utilized in here. Buhwang, one of the alternative medicines, is applying negative pressure to the skin to extract blood or body fluids. Thus in-depth investigation is needed for identify the causality of several suspected factors. It is necessary to investigate the exposure to risk factors for infection and infection period for patients in these regions. Most importantly, whether the exposure is made in the present, and if so, the preventative actions should be carried out immediately.

Although Fig. 3 showed the prevalence in Jeju island to be moderately high, Fig. 4 resulted in the insignificant prevalence

at this region. The APR of Jeju and Seogwipo are bigger than 1 (1.15 and 1.29) but it was not high enough for significantly being the high risk cluster. Nevertheless the prevalence of Jeju needs to be continuously monitored in the future.

The first limitation of this study is that the analyzed data includes only patients who diagnosed at health care institutions. However, Korea has implemented the entire National Health Insurance, and diagnosis of hepatitis C is relatively clear because it is diagnosed through blood. Furthermore this study used serial 5 years data which lead to the reliability of the results being high.

The second limitation of this study is that there are likely to be the differences of hospital visit rate by region or by year. However, the high APR region's accessibility of hospital is not high.

Current hepatitis B in Korea through the 'National Immunization Program' and the 'Prevention of HBV Perinatal Transmission' has achieved a significant reduction in prevalence.<sup>16</sup> However hepatitis C lacks proper epidemiological studies, as well as the prevention policy is about promotional activities only. Recently high success rate of hepatitis C treatment is reported.<sup>17</sup> Therefore, inducing active treatment policy is required through identify the high risk regions and related causes should be blocked though in-depth epidemiological studies in these regions.

The prevalence of diagnosed hepatitis C in Korea remains at a constant level, but significant regional variation appeared. In particular, the prevalence in Busan, Jeonnam, and Gyeongnam was higher, and there are three high risk regional clusters. The ports of Busan are located on the Busan's high risk cluster region. Jeonnam and Gyeongnam's clusters commonly located on the coast and they are adjacent to each other. These results will be important information for effective management of hepatitis C and further investigation will be needed in the future.

## CONFLICTS OF INTEREST

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

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