ORIGINAL ARTICLE

Estimation of Seroprevalence of Hepatitis B Virus and Hepatitis C Virus in Taiwan from a Large-scale Survey of Free Hepatitis Screening Participants

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Background/Purpose: Taiwan is a hyperendemic area of liver diseases. Hepatitis B virus (HBV) and hepatitis C virus (HCV) are the two major etiologies of liver diseases in Taiwan. This study investigated the seroprevalence of HBV and HCV in Taiwan.

Methods: Since 1996, a series of outreach community-based screening programs for liver diseases have been available to the general population aged ≥ 18 years. Blood samples were obtained from the subjects and sent for hepatitis B surface antigen (HBsAg) and antibody to HCV (anti-HCV) tests.

Results: The prevalence of HBsAg(+) was 17.3% (27,210/157,720), while the prevalence of anti-HCV(+) was 4.4% (6904/157,720). Geographic variation in HBV and HCV seroprevalence was found, with the highest anti-HCV positive rate in Miaoli County, Chiayi County, Chiayi City, and Yunlin County, and the highest HBsAg positive rate in Keelung City and Yilan City. The HBsAg positive rate progressively decreased after the age of 50 years, while the anti-HCV positive rate progressively increased after the age of 20 years. The estimated total number of HBsAg carriers in the general population > 20 years old is 3,067,307, while the estimated number of anti-HCV positive patients is 423,283.

Conclusion: This study estimated a 17.3% seroprevalence of HBV and a 4.4% seroprevalence of HCV in Taiwan. Significant geographic variations in the seroprevalence of HBV and HCV were found. These data suggest the importance of modifying programs for the prevention and treatment of chronic viral hepatitis in Taiwan to reflect its varying prevalence and epidemiology. [*J Formos Med Assoc* 2007; 106(2):148–155]

Key Words: geographic variation, hepatitis B virus, hepatitis C virus, screening, seroprevalence, Taiwan

Taiwan is a hyperendemic area of liver diseases.[1] Chronic liver disease and cirrhosis was the sixth leading cause of death in Taiwan in 2002. Cancer was the leading cause of death in Taiwan, and hepatocellular carcinoma (HCC) was the leading cause of death among all cancers in 2002.[2] Hepatitis B virus (HBV) and hepatitis C virus (HCV) are the two major etiologies of liver diseases in Taiwan.[3]

Around 15–20% of adults in Taiwan are chronically infected with HBV.[4] Most chronic carriage of HBV results from infection in early childhood, especially before 2 years of age.[5–7] To control HBV infection, universal HBV immunization was

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started in Taiwan in 1984,[8] which significantly decreased the HBV carrier and infection rates among children and adolescents born after the start of the program. The prevalence of hepatitis B surface antigen (HBsAg) among persons younger than 15 years of age decreased from 9.8% in 1984 to 0.7% in 1999.[9] In addition, the incidence of HCC in children has declined.[10]

In studies reported from 1991 and 1993, the prevalence of antibody to HCV (anti-HCV) in the general population ranged from 0.4–2.5%.[1,11–13] Other studies reported over the period from 1992 to 2003 revealed geographical variations in the seroprevalence of anti-HCV as well as several HCV hyperendemic areas. The seroprevalence of anti-HCV varied from 1.7% to 57.9% in different townships in these studies.[14–19]

The Liver Disease Prevention and Treatment Research Foundation in Taiwan, founded in 1994, initiated screening programs in 1996. As of May 2005, around 160,000 screenings have been performed. The aim of this study was to investigate the seroprevalence of HBV and HCV in Taiwan based on the screening data of the Liver Disease Prevention and Treatment Research Foundation.

Methods

Screening program

The Liver Disease Prevention and Treatment Research Foundation initiated an outreach community-based screening program for liver diseases in 1996. These screenings were open to the general population aged ≥ 18 years. Subjects were invited by mail, radio broadcasts, newspapers and television to go to the screening station. General information, including name, sex, and contact information (including telephone number and address) were recorded. Blood samples were obtained from subjects and sent for aspartate aminotransferase (AST), alanine aminotransferase (ALT), HBsAg, anti-HCV and α-fetoprotein (AFP) tests (General Biologicals Corporation, Hsinchu, Taiwan). Since most people born after 1984 had received HBV vaccination, those subjects were not included in the analysis.

Estimation of patient numbers

To estimate total numbers of HBsAg positive or anti-HCV positive individuals in Taiwan, the following method based on the combined stratifications of city/county and age groups was used. The number of positive individuals in the selected area (city or county) was calculated according to age group. The patient number in a selected area (city or county) = the seropositive rate of an age group × the total population in the corresponding age group in that area. The total number of positive individuals in Taiwan was calculated as the sum of positive individuals in each area. The total population in each age group of an area was obtained from the Department of Statistics of the Ministry of the Interior.[20] Because the population listed by the Department of Statistics of the Ministry of the Interior is grouped in 5-year intervals, and there were few HBV or HCV carriers younger than 20 years old, the estimated number of HBV or HCV carriers was restricted to those older than 20 years.

Follow-up

Screening results were mailed to subjects. Subjects with a positive result for either HBsAg or anti-HCV or those who had elevated AFP or ALT levels were requested to return to the collaborating hospitals for subsequent management.

Results

Estimated seroprevalence of HBV and HCV in Taiwan

From 1996 to June 2005, a total of 164,302 screenings were performed. Analysis by name and birth date revealed that 3988 persons had multiple examinations and 312 records had incomplete name data (either missing surname or missing first name). These 4300 records were excluded. Thus, a total of 160,002 subjects were included in the analysis. The mean age of those subjects was

54.8 ± 15.9 years. Among them, 157,720 subjects were ≥ 20 years old. The subsequent analyses were based on these 157,720 subjects.

The prevalence of positive HBsAg was 17.3% (27,210/157,720), while the prevalence of positive anti-HCV was 4.4% (6904/157,720). Among subjects with available gender data, the HBsAg positive rate was 21.0% (14,171/67,559) in males and 14.0% (11,867/84,600) in females (male *vs.* female, $p < 0.001$). The anti-HCV positive rate was 4.5% (3029/67,559) in males and 4.3% (3611/84,600) in females (male *vs.* female, $p = 0.0412$).

Geographic variation in seroprevalence of HBV and HCV

Geographic variation in HBV and HCV seroprevalence were analyzed in the 157,451 subjects with available data on location of residence. Because of differences in the mean age of the screened subjects among different cities/counties (data not shown), age-adjusted prevalence was used to compare seroprevalence among different cities/counties. The age-adjusted prevalence was estimated using the WHO 2000 standard population as a standard.

As shown in Table 1, the crude seroprevalence of HBV was around 13–25% in different cities or counties. Analysis of age-adjusted HBV seroprevalence showed that Keelung City and Yilan City had the highest HBV seroprevalence, while Penghu County and Taitung County had the lowest HBV seroprevalence.

As shown in Table 2, there was a wide variation in crude HCV seroprevalence, ranging from 0.4% to 10.5%. Analysis of age-adjusted HCV seroprevalence revealed that Miaoli County had the highest HCV prevalence, followed by Chiayi County, Chiayi City, Yunlin County, Tainan County, Kaohsiung City and Kaohsiung County. Kinmen County had the lowest age-adjusted HCV seroprevalence.

Seroprevalence of HBV and HCV in different age groups

To investigate trends in HBV and HCV seroprevalence by birth year, we arbitrarily grouped subjects into 10-year intervals and calculated the HBsAg and anti-HCV positive rate according to birth year. As shown in Figure 1, subjects with birth years 1950–1969 had the highest HBsAg positive rate. The HBsAg positive rate progressively decreased in subjects born before 1950. In contrast to the age trend in HBsAg positive rate, the anti-HCV positive rate progressively increased from birth years 1970–1983 to birth year 1919 (Figure 2). To further delineate HCV seroprevalence in the different age groups, we arbitrarily classified HCV seroprevalence into four categories: ≤ 2.4%, 2.5–4.9%, 5–10%, > 10%. As shown in Table 3, there was no difference in the trends of progressively increasing HCV prevalence after the age of 20 years among the four prevalence categories.

Estimate of total carrier numbers

Due to the finding of differences in the seropositive rate in different city/counties or age groups, we estimated the HBsAg and anti-HCV carrier numbers based on the combined stratifications of city/county and age groups. The estimated total number of HBsAg carriers in the general population > 20 years old in Taiwan was 3,067,307, while the estimated total number of anti-HCV positive carriers was 423,283.

Discussion

This study estimated that in Taiwan as a whole, the prevalence of positive HBsAg was 17.3%, while the prevalence of positive anti-HCV was 4.4%. The HBsAg positive rate was similar to that reported 18 years ago.[4] This finding was not surprising because the study subjects were restricted to persons older than 20 years with birth year before 1984. As universal HBV immunization was started in Taiwan in 1984,[8] subjects older than 20 years comprise the unvaccinated cohort. Previous studies have shown that the prevalence of positive anti-HCV in the general population is around 0.4–2.5%.[1,11–13] Our current study's anti-HCV positive rate is slightly higher than those described before.

Table 1. Seroprevalence (%) of hepatitis B virus (HBV) by birth year estimated from a large-scale survey of volunteers in Taiwan

	1919 and earlier	1920–1929	1930–1939	1940–1949	1950–1959	1960–1969	1970–1983	Crude prevalence	Age-adjusted prevalence
Keelung City	33.3	16.7	25.0	21.2	21.0	30.9	42.9	25.1	29.1
Taipei City	7.4	11.4	14.4	15.2	19.5	18.8	11.7	15.5	15.2
Taipei County	6.3	10.7	15.0	17.6	21.4	21.6	15.8	17.7	19.1
Taoyuan County	7.6	10.6	13.2	19.3	24.0	24.9	12.9	19.0	18.1
Hsinchu City	9.7	10.6	15.6	18.4	23.6	23.5	14.9	18.4	19.1
Hsinchu County	9.7	9.4	13.7	17.9	20.9	23.5	13.0	17.9	15.8
Miaoli County	8.6	10.6	14.1	19.4	21.3	21.0	19.0	17.7	19.4
Taichung City	13.8	10.1	16.1	18.9	25.4	23.2	11.6	20.3	18.7
Taichung County	10.0	13.6	15.9	20.9	25.6	23.8	15.3	20.6	20.0
Changhua County	10.3	13.0	16.0	22.0	24.8	22.8	16.1	20.3	19.9
Nantou County	9.1	7.5	13.9	18.2	19.9	13.7	14.9	15.4	15.0
Yunlin County	6.6	10.2	13.5	16.2	19.0	19.6	16.4	14.9	15.5
Chiayi City	9.1	13.6	15.6	18.7	23.7	21.3	17.0	18.2	19.0
Chiayi County	8.7	13.2	16.4	19.8	22.8	24.7	11.1	17.9	17.8
Tainan City	6.7	11.0	12.4	16.7	20.1	15.7	16.5	15.3	15.3
Tainan County	9.5	10.3	15.0	17.1	18.9	22.7	15.3	16.8	15.9
Kaohsiung City	12.1	11.0	16.3	19.6	20.4	21.8	18.2	18.8	18.9
Kaohsiung County	7.7	9.0	10.9	17.1	19.2	20.4	17.5	16.1	16.7
Pingtung County	6.3	9.7	13.6	14.8	18.1	20.5	13.7	14.8	15.5
Yilan County	23.7	22.9	20.6	33.3	42.9	46.7	15.4	23.2	31.6
Hualien County	8.4	9.7	12.8	17.4	19.0	20.8	24.0	17.0	18.8
Taitung County	5.8	9.0	10.4	12.8	18.6	19.8	8.8	13.0	12.5
Penghu County	9.8	11.6	11.8	14.9	14.4	14.6	11.2	13.2	11.6
Kinmen County	6.5	10.7	19.1	17.4	23.7	22.2	9.1	19.0	15.9

Table 2. Seroprevalence (%) of hepatitis C virus (HCV) by birth year estimated from a large-scale survey of volunteers in Taiwan

	1919 and earlier	1920–1929	1930–1939	1940–1949	1950–1959	1960–1969	1970–1983	Crude prevalence	Age-adjusted prevalence
Keelung City	16.7	29.2	0	0	1.2	2.5	0	3.8	2.3
Taipei City	4.5	3.3	3.2	1.8	1.5	0.4	0	2.0	1.2
Taipei County	4.6	4.7	3.5	1.9	1.3	0.7	0.5	2.1	1.4
Taoyuan County	6.0	6.2	4.4	4.7	2.0	0.9	0	3.3	2.3
Hsinchu City	10.2	11.3	7.8	4.3	1.7	1.0	0.2	4.5	2.7
Hsinchu County	9.0	6.9	4.7	4.1	2.0	1.2	1.0	3.4	2.3
Miaoli County	22.8	17.3	10.9	11.8	8.0	5.6	3.2	10.5	7.6
Taichung City	13.8	7.4	5.7	5.4	1.7	1.2	0.8	3.6	2.8
Taichung County	14.8	9.4	6.8	4.1	2.1	1.3	0	4.1	3.1
Changhua County	6.2	8.5	5.8	5.3	2.4	1.5	0.5	4.1	2.8
Nantou County	3.4	7.5	5.2	5.7	1.8	0.6	0	3.7	2.3
Yunlin County	16.1	14.1	11.2	7.4	3.4	1.4	1.8	8.3	4.8
Chiayi City	17.7	19	13.6	11.3	4.5	2.1	0.7	9.8	6.0
Chiayi County	17.2	18.8	12.7	11.0	5.6	2.4	2.4	10.3	6.1
Tainan City	8.9	7.1	5.2	3.4	1.4	1.1	0.5	3.6	2.0
Tainan County	14.7	15.4	10.0	6.6	1.8	2.2	1.1	6.4	4.0
Kaohsiung City	9.3	11.2	8.0	4.8	3.2	2.5	1.3	4.6	3.8
Kaohsiung County	8.3	9.2	8.0	5.0	3.2	1.9	1.4	4.8	3.5
Pingtung County	3.3	3.9	1.9	1.9	1.5	0.7	0.2	1.9	1.2
Yilan County	5.0	5.1	5.2	3.3	0	0	0	4.8	0.8
Hualien County	15.2	12.9	9.5	5.0	3.5	1.3	0.3	5.6	3.7
Taitung County	8.4	6.1	6.6	3.4	2.1	1.2	0	4.3	2.4
Penghu County	15.6	13.4	9.0	3.1	2.6	0.6	0	6.0	3.0
Kinmen County	0	1.8	0	0.3	0.8	0	0	0.4	0.3

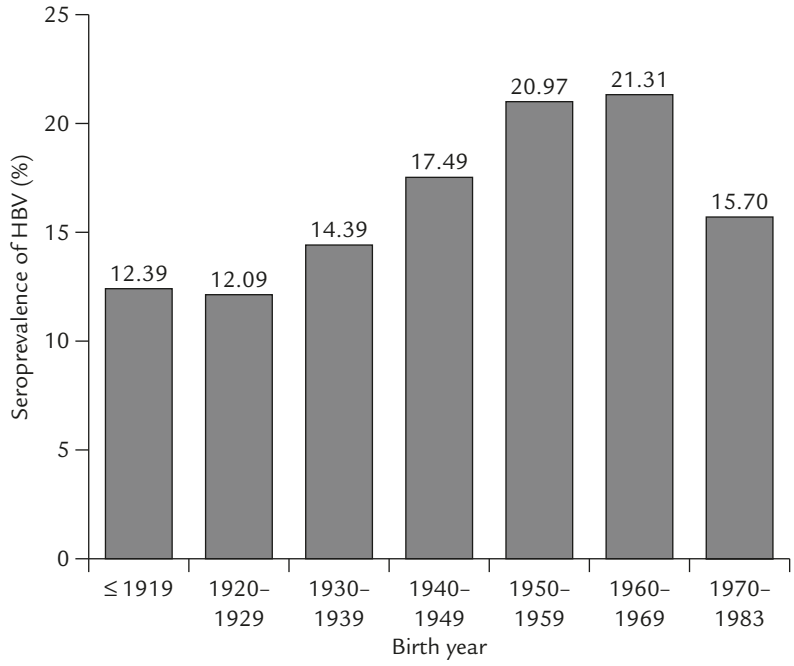

Figure 1. Birth year-adjusted seroprevalence of hepatitis B virus (HBV) estimated from a large-scale survey of free hepatitis screening participants in Taiwan.

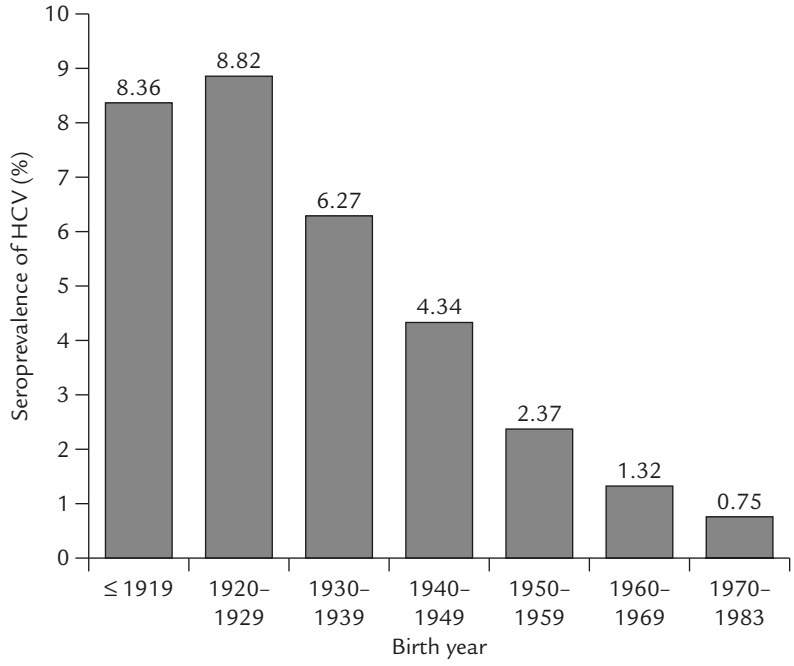

Figure 2. Birth year-adjusted seroprevalence of hepatitis C virus (HCV) estimated from a large-scale survey of free hepatitis screening participants in Taiwan.

There were geographic variations in both HBV and HCV seroprevalence in Taiwan. The reasons for the geographic variations in the seroprevalence of HBV are not known. Sampling bias may be one of the possible explanations. For example, in Keelung City, the HBsAg positive rate in birth years 1970–1983 was 42.9%, which was significantly higher than the HBsAg positive rates of the same birth years in other areas. Therefore, we cannot rule out the possibility that the screened subjects in Keelung might contain a certain proportion of HBV carriers, thus leading to the higher HBV seroprevalence in Keelung. Regarding the anti-HCV positive rate, our study clearly showed that

Table 3. Seroprevalence of hepatitis C virus (HCV) according to age and different prevalence rates

Age group (yr)	HCV prevalence (%)			
	≤2.4	2.5–4.9	5–10	>10
20–24	0	0.8	0.4	3.1
25–29	0.3	0.7	1.0	1.6
30–34	0.5	1.2	1.9	4.1
35–39	0.7	1.7	1.5	3.9
40–44	1.1	1.6	2.1	5.4
45–49	1.3	2.8	3.3	7.2
50–54	1.8	4.0	5.8	8.9
55–59	2.0	4.5	7.6	12.4
60–64	2.4	5.9	8.4	12.7
65–69	2.6	7.1	12.3	9.6
70–74	3.4	7.9	14.2	14.8
75–79	3.9	8.3	14.9	19.2
80–84	4.2	6.6	13.5	20.6
85–89	4.1	6.8	16.4	17.8
>90	3.8	8.0	17.9	16.7

there were wide differences in HCV seroprevalence between different areas. Previous studies have shown that there are several high HCV infection areas in Taiwan.[21] The high HCV prevalent areas identified in our study are consistent with previous findings. The HCV hyperendemic areas might be related to the iatrogenic routes. The local culture and medical seeking-behaviors, such as frequent intravenous injection for minor diseases or incomplete disinfection of medical equipment in the past, might contribute to the high HCV prevalence rate.[16,22] However, the real causes of the high HCV prevalence in Miaoli, Yunlin and Chiayi, etc., remain to be investigated.

It was interesting that HBV prevalence progressively declined in subjects with birth years before 1950 (i.e. about after 50 years old). At least two reasons could explain this observation. First, since the peak age of advanced HBV-related liver diseases is 50–60 years, it is probable that some HBV carriers had died of liver-related diseases after 50 years old. Thus, the percentage of HBsAg positivity declined. Second, it has been shown that delayed HBsAg clearance contributes to decreased prevalence of HBsAg.[23,24] Contrary to the trend of HBsAg, the anti-HCV positive rate progressively increased after 20 years old, similar to that found previously in a smaller scale study.[22] The progressive increase in HCV seroprevalence with increased age were found in different areas with different rates of HCV seroprevalence. This observation is also compatible with the concept that HCV infection is acquired in adulthood.

In addition to seroprevalence, one important issue for controlling viral hepatitis is disease burden. Thus, we estimated the patient numbers based on our results. Because there were variations in seroprevalence among townships, the best way to estimate total patient numbers was to use the township-specific seroprevalence. Unfortunately, we did not screen every township of each county or city. Therefore, we did not have detailed township-specific seroprevalence. So, we used city/county seroprevalence instead. In the general population older than 20 years, we estimated a total of 3,067,307 HBsAg carriers, and a total of 423,283 anti-HCV positive patients. These data could help us with resource allocation in controlling viral hepatitis in Taiwan.

However, there were drawbacks to our current study. Since the open screening program relied on subjects volunteering to come forward of their own volition, the screened population might not represent the true general population in Taiwan. It is possible that more sick than healthy people participated, leading to an overestimation of the prevalence of HBsAg and anti-HCV. Nevertheless, our data constitute a useful reference for the prevention and treatment of viral hepatitis in Taiwan.

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