Ethnic-specific Prevalence of Hepatitis B/C Virus Infection in Pin-Jen, Taiwan

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Objectives: The study aimed to estimate prevalence rate of hepatitis B/C virus infection by three ethnic groups including Hakka, Minnan, and Mainlander in Taiwan where there was a high incidence of hepatocellular carcinoma.

Methods: We enrolled a total of 5007 people aged 30 years or older who participated in Li-Shin Out-Reaching Neighboring Screening (LIONS) project in 2004–2005 in Pin-Jen township of Taoyuan county. The ethnic group was classified in the current study by using the criteria on the basis of the ethnicity of mother of participants. We collected the character of participants, hepatitis B/C virus infection, and life-style factors for the comparison across three ethnic groups.

Results: The highest positive rate of hepatitis B virus infection was seen in Minnan descendants (15.1%), followed by Hakka descendants (11.4%), and Mainlander descendants (6.6%). The difference by three groups was statistically significant (*P*<.001). Positive hepatitis B virus infection declined with age whereas positive hepatitis C virus infection increased with age regardless of ethnic group. By using ecological analysis, the higher proportion of Minnan was positively correlated to the elevated incidence of hepatocellular carcinoma (HCC) (correlation coefficient=.46, *P*=.03).

Conclusions: Our population-based study shows prevalence rate of hepatitis B and C virus infection varies with ethnic group, with higher rate in Minnan. This finding was consistent with the ecological result, the higher the composition of Minnan the higher the incidence of HCC. (*Ethn Dis.* 2009;19:384–389)

Key Words: Ethnic, Hepatitis, Hakka, Chinese, Hepatocellular Carcinoma

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Introduction

Hepatocellular carcinoma (HCC) incidence and mortality have been reported at high rates in Southeast Asia and Sub-Saharan Africa and at low rates in most Western countries. Such geographical variation has been explained by three recognized risk factors for HCC[1–4]: hepatitis B virus (HBV) infection,[5–7] hepatitis C virus (HCV) infection[5–8] and aflatoxin exposure.[9–11] The prevalence of chronic HBV infection was found higher in developed countries than developing countries.[12] A wide variation of HBV infection has also been seen in the Asia-Pacific region.[12] Using data available from 22 European countries, the areas of low prevalence for HCC, geographical difference in HCV infection has also been demonstrated to be correlated with geographic variation of HCC mortality.[8] Chin et al reported Asian patients with HCC had poorer survival rates than non-Asian patients.[13] The ethnic difference in the seroprevalence of HBsAg has been reported as 6% in Uygur, 9% in Kazak and 12% in Han populations. These finding may suggest that geographic variation may be a reflection of ethnic/racial difference.

High prevalence of hepatitis B and C infections have been reported in Taiwan, an area of high prevalence for HCC. However, little is known about whether hepatitis B/C virus infection varies across sub-ethnic groups in this high-risk population. We aimed to estimate prevalence rate of hepatitis B/C virus infection in three ethnic groups in Taiwan: Hakka, Minnan, and Mainlander.

Methods

Study population

The study subjects were derived from Li-Shin Out-Reaching Neighboring Screening (LIONs). The program was described in detail elsewhere.[14] Briefly, the program's goal is to promote the early detection of three common chronic diseases among adults aged $\geq$30 years: type 2 diabetes, hypertension, and hyperlipidemia. The preventive service model was modified from an integrated multiple community-based screening model developed in Keelung (KCIS).[15,16] A total of 7,872 participants were enrolled in the LIONS project in 2004–2005 in Pin-Jen Township of Taoyuan County. After excluding 2,469 participants without information on hepatitis virus infection, 105 participants without information on ethnicity, 96 aboriginal participants, and 195 participants who were double tested, 5,007 subjects were available for our analysis.

Definition of ethnic group

Information on ethnic group was acquired by face-to-face interview about the ethnicity of each participant's parents. We only considered mother-child consanguinity and excluded adopted relationships, partly because vertical transmission may play an important role in acquiring a hepatitis B virus infection and partly because the lifestyle of Taiwanese people has been predominantly affected by the mother.

Data collection

Hepatitis B/C virus infection was tested by using the ELISA method, assessing the presence of HBsAg acquired in childhood or early adulthood and anti-HCV. Data on lifestyle factors were collected by well-trained nurses

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with face-to-face interviews using a structured questionnaire. Relevant variables included smoking, alcohol consumption, and betel quid chewing with three classifications: current user, ex-user, and non-user.

Ethnicity and Incidence of Hepatocellular Carcinoma (HCC)

As hepatitis B/C virus infections are two major risk factors responsible for HCC, we tested whether the composition of ethnic group and the incidence of HCC in 25 administrative regional areas in Taiwan were highly correlated. We excluded Matsu area, an offshore island, with a small population size.

Statistical Analysis

Positive rate of hepatitis B virus infection was presented by percentage. Logistic regression was used to estimate odds ratios of having HBV/HCV virus infection, with adjustment of age, sex, smoking, drinking, and betel quid chewing. Correlation analysis was performed to assess the correlation between the composition of ethnic group and the incidence of HCC. Statistical significance was determined with P value less than .05.

RESULTS

Table 1 shows the positive rate of hepatitis B/C virus infection by ethnic group. The highest positive rate of hepatitis B virus infection was seen in Minnan descendants, followed by Hakka descendants, and Mainlander descendants ($P<.001$), particularly in subjects aged ≤60 years. In contrast, the overall difference in positive rate of hepatitis C virus infection across the three ethnic groups was not statistically significant ($P=.21$) but the corresponding findings were significant in subjects aged 50–59 years and 70–79 years. A lacking of statistical significance across the three groups in subjects aged 60–69 years may be attributed to fewer cases. By combining subjects aged ≥50 years, the difference across the three groups was statistically significant ($P=.01$). Figure 1 shows that only a small fraction of participants, regardless of ethnic group, had both hepatitis virus infections.

This finding was further supported by data that show both hepatitis virus infections by age groups (Figure 2). The rate of positive hepatitis B virus infection declined with age whereas the rate of positive hepatitis C virus infection increased with age regardless of ethnic group.

The descendants of Hakka and the Minnan had approximately 2-fold (1.50–2.95) and 1.67-fold greater likelihood, respectively, of having a hepatitis B virus infection when compared with Mainlander descendants(Table 2). The effect declined with increasing age (data not shown). Females were significantly more likely to have a hepatitis B virus infection. There were no significant associations between smoking, alcohol, and betel quids and a positive rate of hepatitis B virus infection in univariate or multivariate analysis.

For the hepatitis C virus infection, the descendants of Hakka and the Minnan had approximately 2.64-fold (1.49–4.66) and 2.02-fold (1.17–3.48) greater likelihood respectively, of being infected when compared with Mainlander descendants (Table 3). The effect increased with increasing age. Males were significantly more likely to have the infection. Current smokers had a significantly greater risk (two-fold) for

Table 1. Age-specific positive rate of HbsAg and/or anti-HCV by different ethnic groups

Age groups	Hakka	Minnan	Mainlander	Total	P
		HBsAg positive rate % (*n*)			
30–39	12.2 (490)	16.5 (664)	7.8 (102)	14.1 (1256)	.01
40–49	13.4 (604)	15.0 (453)	6.6 (106)	13.4 (1163)	.07
50–59	10.2 (508)	15.6 (377)	10.4 (115)	12.3 (1000)	.04
60–69	11.7 (391)	13.1 (221)	5.0 (60)	11.6 (672)	.21
70–79	7.4 (175)	9 (100)	6.2 (466)	6.8 (741)	.57
≥80	3.3 (30)	5.5 (18)	4.2 (118)	4.2 (166)	.93
Total	11.4 (2201)	15.1 (1839)	6.6 (967)	11.8 (5007)	<.001
		Anti-HCV positive rate % (*n*)			
30–39	1.6 (490)	1.9 (664)	0.0 (102)	1.6 (1256)	.35
40–49	3.4 (604)	1.9 (453)	0.9 (106)	2.6 (1163)	.17
50–59	2.1 (508)	5.5 (377)	2.6 (115)	3.5 (1000)	.02
60–69	5.1 (391)	5.4 (221)	0.0 (60)	4.7 (672)	.19
70–79	11.4 (175)	13.0 (100)	2.7 (466)	6.2 (741)	<.001
≥80	10.0 (30)	5.5 (18)	6.7 (118)	7.2 (166)	.79
Total	3.73 (2201)	3.62 (1839)	2.52 (967)	3.6 (5007)	.20
		HBsAg and Anti-HCV positive rate % (*n*)			
30–39	0.4 (490)	0.1 (664)	0.0 (102)	0.2 (1256)	.59
40–49	0.1 (604)	0.0 (453)	0.0 (106)	0.05 (1163)	.62
50–59	0.5 (508)	0.2 (377)	0.0 (115)	0.4 (1000)	.57
60–69	0.7 (391)	0.4 (221)	0.0 (60)	0.5 (672)	.72
70–79	2.2 (175)	2.0 (100)	0.0 (466)	0.8 (741)	<.00
≥80	0.0 (30)	5.5 (18)	0.0 (118)	0.6 (166)	.01
Total	0.37 (2201)	0.22 (1839)	0.00 (967)	0.4 (5007)	.04

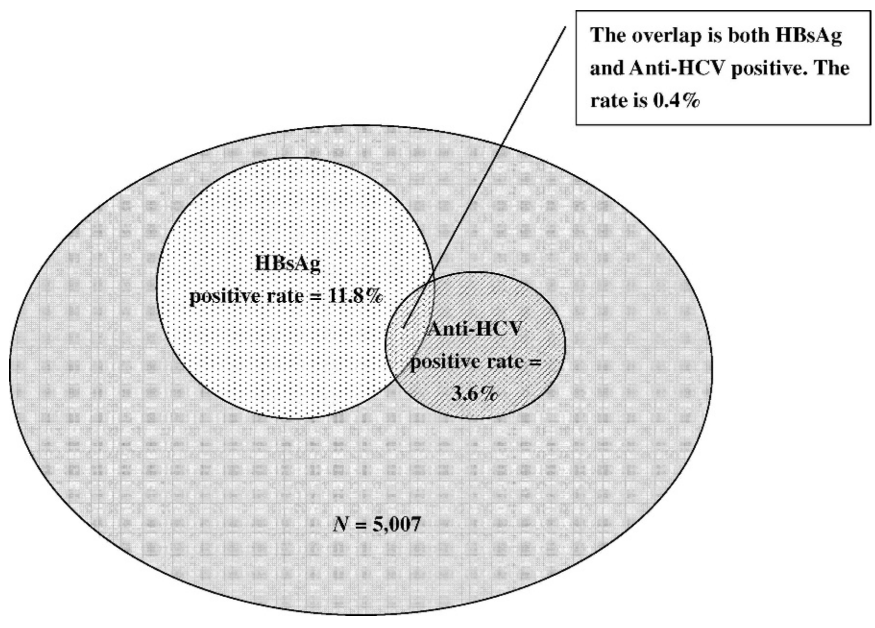

Figure 1. The HBsAg and anti-HCV postitive rate

having a hepatitis C virus infection compared with non-smokers. No significant associations were found between alcohol and betel quids and the chance of having a hepatitis C virus infection.

Figures 3a–3c show the results of correlation between the composition of each ethnic group and the incidence of HCC by 25 regional areas. The larger the proportion of Minnan in the population, the greater the incidence of HCC. A linear and positive relationship for the Minnan was statistically significant (r=.46, P=.03). There was no significant positive associations for the other two ethnic groups.

DISCUSSION

Using the data from a community-based survey, the prevalence rates of hepatitis B/C virus infection were compared across the descendants of three ethnic groups in Taiwan. We found the Hakka and the Minnan group had a higher likelihood of having hepatitis B/C virus infection than the Manlainder group. The difference in hepatitis B virus infection was predominantly seen in younger age groups whereas the disparity of hepatitis C

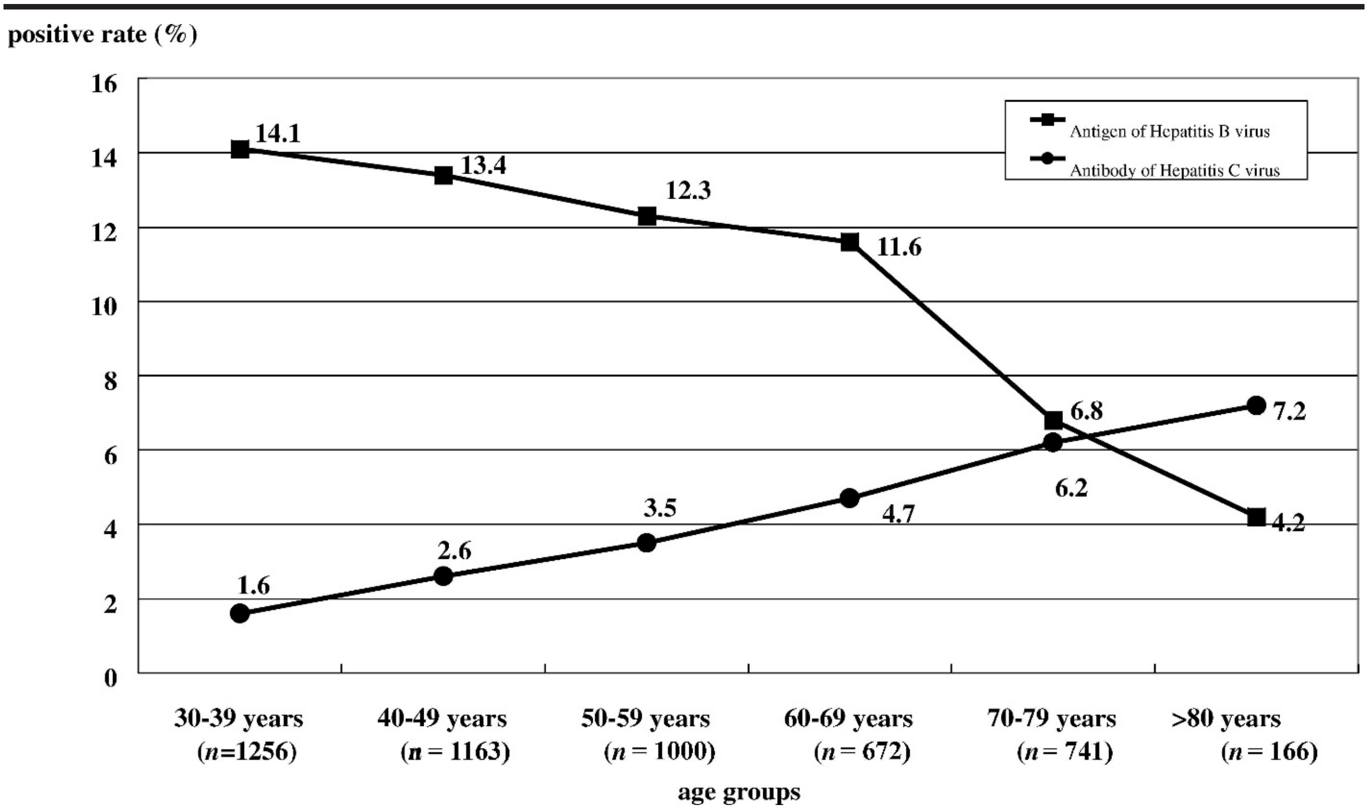

Figure 2. Age-specific prevalence rate of HBsAg and anti-HCV

Table 2. Multivariate logistic regression analysis of risk factors for subjects with positive antigen to Hepatitis B virus

Variable	Group/ inference group	Number	Odds Ratio	Adjusted Odds Ratio	95% CI
Age		5,007	0.98	0.98**	0.97–0.99
Sex	male / female	1,774 / 2,573	0.88	0.74*	0.58–0.93
Ethnic	Hakka / Mainlander	1,619 / 866	2.51	2.10**	1.50–2.95
	Minnan / Mainlander	1,862 / 866	1.83	1.67**	1.21–2.33
Smoking	ex-smoker / never smoking	295 / 3,441	0.99	0.99	0.72–1.37
	current smoking / never smoking	611 / 3,441	1.32	1.34	0.91–1.99
Alcohol	quit drinking / never drinking	166/ 3,470	0.98	0.86	0.65–1.15
	current drinking / never drinking	711 / 3,470	0.82	0.76	0.44–1.33
Betel	ex-user / never use	124 / 4,138	0.99	0.77	0.38–1.57
	current user / never use	85 / 4,138	1.30	1.00	0.58–1.72

* $P<.05$; ** $P<.01$

virus infection was demonstrated more in the older age groups.

A high correlation between the composition of ethnic group and HCC incidence rate by county was also observed by ecological analysis.

Comparison of prevalence in different ethnic groups

In Taiwan, the overall prevalence rates of hepatitis B infection, hepatitis C infection, and both infections for inhabitant aged 30 years or older were 14.7%, 4.6%, and 0.4%, respectively.[17] The hepatitis C virus infection prevalence rates vary from region to region in Taiwan, from 5.1% in Ilan county,[18] 7.6% in Hsin-chu,[4] and up to 50.3% in Kaoshung, the capital city of southern Taiwan.[19] Similar findings, to a lesser extent, were also found for hepatitis B virus infection with a range between 15% and 20%.[16,20–22] In the United States, the Rochester Epidemiology project found that after controlling for age and sex, the prevalence rate of hepatitis B virus infection was 0.15%, with the highest rate in Asian immigrants (2.1%) and the lowest in Caucasians, 0.02%).[20] As mentioned above, such geographic variation may be attributed to ethnic/racial differences. Very few studies have emphsized the ethnicity-specific prevalence rate of hepatitis B virus infection. A small study in the Hsin-Chu area showed an average rate of 7.6% hepatitis C virus infection with the highest in the Minnan group (12.1%) followed by the Hakka group (8%) and the lowest in Tayal aboriginal group (6.3%).[4] However, the difference was not statistically significant. The result may be unreliable because of sparse data, particularly among the Minnan and aboriginal groups. However, other studies on aboriginal groups found the rates were higher among Bunun and Tayal aboriginal groups in Hualien county, with rates of of 15.2% and 14.2%, respectively.[23] Similar findings were found in another study (16.9%).[21]

The finding that the difference in hepatitis B virus infection was predominantly seen in the young age group may be attributed to the fact that hepatitis B virus infection is frequently acquired in childhood partially due to vertical transmission and partially due to horizontal transmission before 20 years of age. In contrast, the difference in hepatitis C virus infection was in the older age groups. The prevalence rate of hepatitis C virus infection increased with age in our study, which was consistent with the finding in a previous

Table 3. Multivariate logistic regression analysis of risk factors for subjects with positive antibody to Hepatitis C virus

Variable	Group/ inference group	Number	Odds Ratio	Adjusted Odds Ratio	95% CI
Age		5007	1.03	1.05**	1.03–1.064
Sex	male / female	1774 / 2573	1.04	1.83*	1.12–2.95
Ethnic	Hakka / Mainlander	1619 / 866	1.46	2.64**	1.49–4.66
	Minnan / Mainlander	1862 / 866	1.47	2.03*	1.17–3.48
Smoking	ex-smoker / never smoking	295 / 3441	1.28	1.51	0.83–2.70
	current smoking / never smoking	611 / 3441	1.69	2.14*	1.08–4.22
Alcohol	quit drinking / never drinking	166/ 3470	1.19	1.22	0.71–2.07
	current drinking / never drinking	711 / 3470	1.66	1.05	0.43–2.50
Betel	ex-user / never use	124 / 4138	1.22	2.19	0.71–6.70
	current user / never use	85 / 4138	1.40	1.82	0.72–4.59

* $P<.05.$; ** $P<.01$

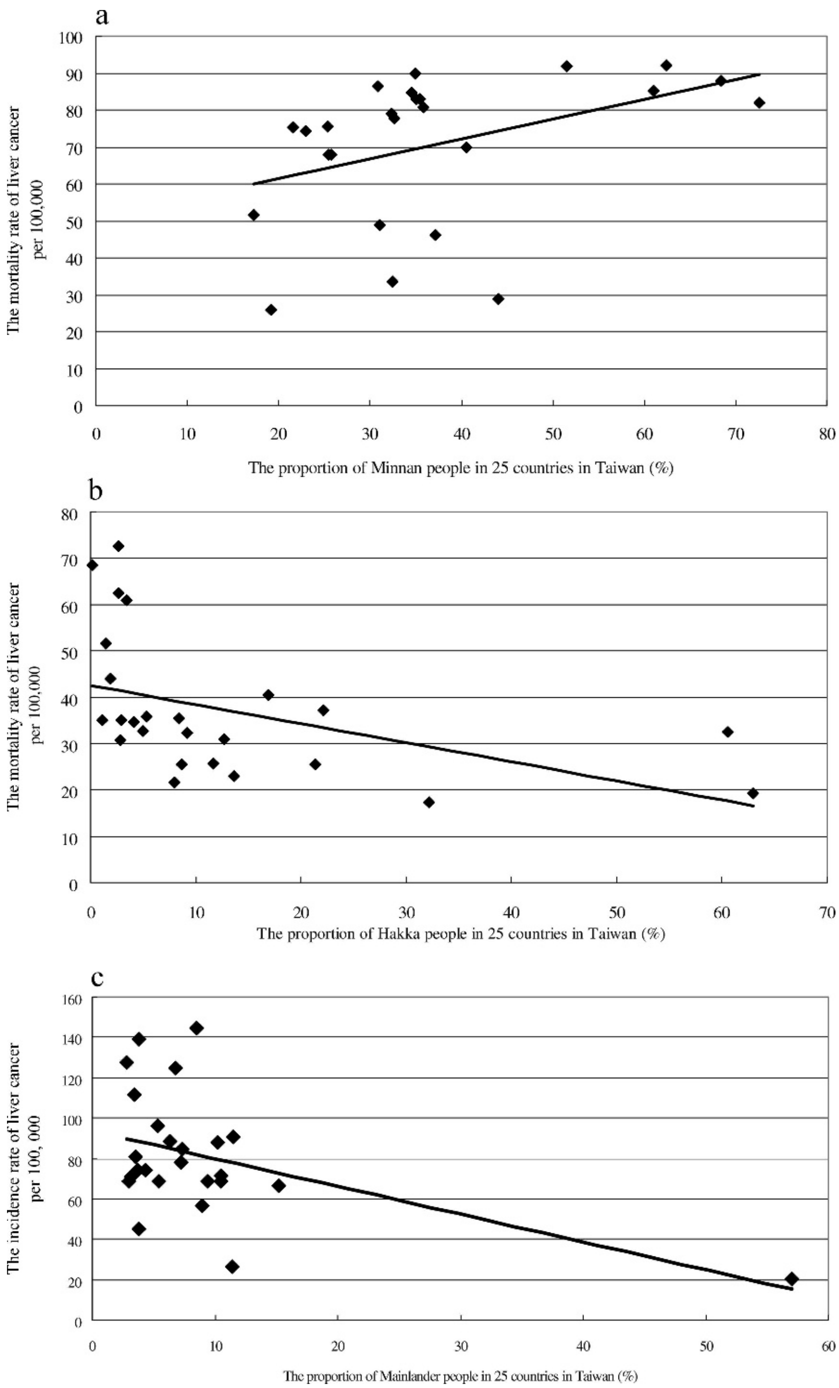

Figure 3. The correlation between the composition of each ethnic group and HCC incidence by 25 areas in Taiwan

study.[4] Another study in Ilan found subjects aged 60 years had a two-fold increased risk for hepatitis C virus infection compared with those aged <60 years.[18] One possible cause of the higher prevalence rates of hepatitis C virus infection in the elderly compared with the young may be that, in the early 1970s, elderly people were inadvertently injected with a used syringe needle when they sought medical care.[4,19]

Implication for early detection and clinical management

Information on ethnic-specific prevalence rates of hepatitis B/C virus infection may be very helpful in assessing the prognosis of HCC and aiding health policy decision makers in allocating resouces for early detection of HCC. A previous study has already shown that Asian patients diagnosed with HCC had a much worse prognosis than non-Asian patients.[13] Whether the Minnan group had poor survival rates compared with the two other groups deserves further investigation. From the viewpoint of preventive medicine, our study suggests, given limited resources, early detection of HCC (ie, screening for HCC) should be taken as the first priority for the Minnan descendants.

There are several limitations in the current study. Since our study subjects were aged ≥30 years, it could be argued that HBV or HCV infection may be underestimated because of the exclusion of study subjects aged 30 years or below. For HBV infection, the impact is minor because the majority of HBV infections in adults were acquired in childhood before the era of nationwide universal vaccination. Most adults aged <30 years who had the HBV vaccine had relatively lower HBV infection rates. For HCV infection, whether the exclusion of younger subjects leads to biased result is difficult to assess. However, as HCV infection is related to the improvement of medical care and sanitary conditions, HCV infection may have sharply declined in the younger generation. Secondly, the disparity of HBV and HCV infection across ethnic groups cannot be fully corroborated in the current study because the association between ethnic/racial group and HBV or HCV infection may be attributed to the fact that certain ethnic groups may be susceptible to infection due to certain specific genetic markers. Or, HBV or HCV infections may cluster in certain ethnic groups due to poor sanitary conditions, or transmission of HBV or

Our population-based study shows prevalence rate of hepatitis B and C virus infection varies with ethnic group, with higher rates in Minnan descendants.

HCV infections through needle sharing during IV injections.

In conclusion, our population-based study shows prevalence rate of hepatitis B and C virus infection varies with ethnic group, with higher rates in Minnan descendants. This finding was in agreement with the result indicating a higher proportion of Minnan descendants had a higher likelihood of HCC.

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