

Diversity of Hepatitis C Virus Genotypes Among Intravenous Heroin Users in Taiwan

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Abstract: *Introduction:* Limited information is available about genotypes of hepatitis C virus (HCV) in intravenous heroin users in Taiwan. The purpose of this study was to examine the concordance of the detection of antibody to HCV and HCV-RNA and to determine the distribution of HCV genotypes in male intravenous heroin users. *Methods:* This was a cross-sectional study. The study population included 274 intravenous heroin drug users newly sentenced in a male prison in central Taiwan from November 2004 to February 2005, whose antibodies to HCV were positive, and antibodies to human immunodeficiency virus were negative. The mean age was 33.9 years (standard deviation, 7.8). The molecular diagnosis used to identify HCV-RNA was PCR. *Results:* Among 274 subjects, 214 subjects were found to contain HCV-RNA. Positive predictive value of HCV infection using antibody to HCV as an indicator was 78.1%. Among 214 subjects, HCV genotype 2a was the most predominant (58.9%, n = 126), followed by 1a (17.3%, n = 37), 1b (14.5%, n = 31), 2b (8.9%, n = 19) and 1a + 2b (0.4%, n = 1). Age-specific analysis also showed genotype 2a was the most prominent genotype among the 4 age groups, with the highest prevalence in groups aged 20 to 29 years and 30 to 39 years (53.3% and 67.6%, respectively). *Conclusions:* The concordance of antibody to HCV and HCV-RNA is remarkable in selected high-risk groups. HCV genotype 2a is the most prevalent in male intravenous heroin users in central Taiwan, especially in aged 20 to 29 years and aged 30 to 39 years.

Key Indexing Terms: Hepatitis C; Heroin; Genotype; Intravenous drug users. [Am J Med Sci 2011;341(2):110–112.]

In 2008, chronic liver disease and liver cirrhosis were the seventh leading causes of death in Taiwan.¹ Hepatitis C virus (HCV) infection is one of the most commonest causes of these chronic liver disease.^{2–4} Most HCV infections develop into chronic hepatitis, and only 15% to 20% of the infections resolve spontaneously.^{5,6} Several studies have concluded that the HCV genotype plays a key role in determining the prognosis of HCV infection.^{7–10} HCV genotype 1b seems to be more prevalent than other genotypes in patients with severe liver diseases, such as cirrhosis and hepatocellular carcinoma.^{11–13}

HCV has become a critical public health threat. To date, many studies for HCV genotype distributions of the general population in Taiwan have been conducted. In a study by Wu et al¹⁴ in Taiwan, type 2 is the highest prevalence. In a study by Yu et al¹⁵ in southern Taiwan, genotype 1b seems to be more prevalent. In a study by Liou et al¹⁶ in Kinmen islands of

Taiwan, genotype 2a seems to be more prevalent.¹⁶ However, previous studies have reported that specific risk populations, including prison inmates and intravenous drug users, have high prevalence rates of HCV infection.^{17–20} To date, research focusing on the distribution of HCV genotypes in incarcerated intravenous drug users in Taiwan is limited. In a study by Liu et al²¹ among human immunodeficiency virus (HIV)-infected injection drug users in Taiwan, the main genotypes are as follows: 1a, 6a, 3a and 1b. In a study by Lee et al²² among HIV-infected injection drug users in Taiwan, genotype 1b is the most common subtype. There is high variation about HCV genotype distribution. Therefore, it is critical to understand HCV genotypes in these high-risk populations to predict clinical outcomes. This study used data collected from male prisoners in central Taiwan, who have used intravenous heroin before entering the prison, to explore the following questions: (1) What is the association between the presence of antibody to HCV and HCV-RNA in this study population? (2) What is the distribution of HCV genotypes? (3) What is the age-specific prevalence of HCV genotypes?

MATERIALS AND METHODS

Study Population

This was a cross-sectional study. All newly sentenced prisoners older than 20 years within a male prison in central Taiwan from November 2004 to February 2005 were informed that they would receive routine blood checkups and a face-to-face interview by the doctors. In total, 274 intravenous heroin users were enrolled in the study, whose antibodies to HCV were positive and antibodies to HIV were negative. The institutional review board of this medical center approved this retrospective study.

Laboratory Tests

Antibody to HCV (anti-HCV) was detected by the third-generation enzyme immunoassay test (Ortho-Clinical Diagnostics; Rochester, NY). Qualitative detection of serum HCV with LightCycler PCR (LightCycler RNA Amplification Kit SYBR Green I, Roche Applied Science; Mannheim, Germany) was performed as described within the literature.²³ Determination of genotypes by nucleotide sequencing was performed as described within the literature.²⁴

Statistical Analysis

We used the SAS software to analyze data with 2-sided χ^2 test (version 9.1; SAS Institute, Cary, North Carolina). A *P* value <0.05 was considered statistically significant.

RESULTS

Association Between Anti-HCV and HCV-RNA

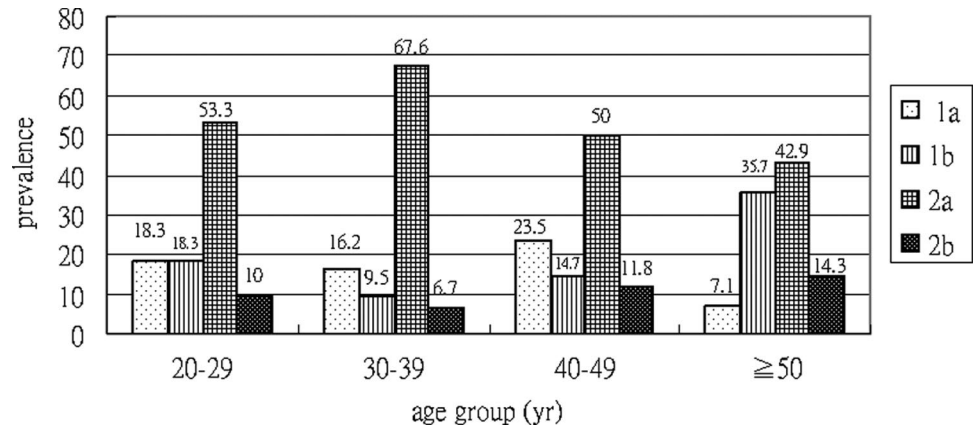
The mean age was 33.9 ± 7.8 years, ranging from 21 to 66 years. Among 274 subjects, 214 subjects were found to contain HCV-RNA. Positive predictive value of HCV infection

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FIGURE 1. Age-specific prevalence of HCV genotypes in male intravenous heroin users in central Taiwan.



using antibody to HCV as an indicator was 78.1% (214 of 274). The concordance of antibody to HCV and HCV-RNA was high.

Distribution of HCV Genotypes

Among 214 subjects, there were 60 subjects aged 20 to 29 years, 106 subjects aged 30 to 39 years, 34 subjects aged 40 to 49 years and 14 subjects aged 50 years and older. Among 214 subjects, genotype 2a (58.9%, $n = 126$) was the most prevalent, followed by 1a (17.3%, $n = 37$), 1b (14.5%, $n = 31$), 2b (8.9%, $n = 19$) and 1a + 2b (0.4%, $n = 1$).

Age-Specific Prevalence of HCV Genotypes

Age-specific prevalence of HCV genotypes was further analyzed. As shown in Figure 1, genotype 2a was the most prominent genotype among the 4 age groups, with the highest prevalence in groups aged 20 to 29 years and 30 to 39 years (53.3% and 67.6%, respectively). By using the 2-sided χ^2 test, there was a significant difference between the prevalence of genotypes and age only in the groups aged 20 to 29 years and 30 to 39 years ($P = 0.011$ and $P < 0.0001$, respectively) but not found in the groups aged 40 to 49 years and 50 years and older ($P = 0.146$ and $P = 0.437$, respectively). However, there was no trend between the prevalence and age groups.

DISCUSSION

Because the prison in Taiwan is uniquely tight to contraband, prisoners are absolutely not allowed to use any illegal drugs after entering the prison. The subjects included in this study were all newly sentenced prisoners. Thus, it is relatively sure that HCV was acquired outside the prison. In this study, positive predictive value of HCV infection using antibody to HCV is 78.1%. That is, the concordance of antibody to HCV and HCV-RNA is remarkable in selected high-risk groups. As prior studies have concluded, populations at greater risk should be routinely tested for antibody to HCV.²⁵ Therefore, we also suggest that testing for antibody to HCV is a valid and cost-efficient screening tool for intravenous heroin users in Taiwan.

HCV genotype 1b has been reported as predominant in patients infected by blood transfusion or unknown risk factors in previous studies.^{12,26-28} However, in a study by Liu et al,²¹ the main genotypes are as follows: 1a (29.2%), 6a (23.5%), 3a (20.2%), 1b (13.2%) and 2b (6.6%). Genotype 2a accounts only for 1.6%.²¹ In a study by Lee et al,²² the major genotypes are as follows: 1b (26.7%), 6a (23.9%), 1a (11.7%), 3a (6.1%), 2a (3.3%) and 2b (3.3%). In this study, the predominant genotype detected in male intravenous heroin users without HIV is 2a

(58.9%), followed by 1a (17.3%), 1b (14.5%) and 2b (8.9%). In particular, HCV genotypes 3 and 4 are not detected. According to the literature review and our finding, a relative diversity of HCV genotypes exists in the population studied, depending on the geographic origin and the underlying risk factors. In a systemic review by Yu and Chuang²⁹, the Asians with genotype 2 have higher sustained virological response than the white when treated with the recommended regimens of standard dose and duration. The response rate is approximately 90%.²⁹ Therefore, it should be suggested to routinely check the genotypes among intravenous drug users with HCV antibody positive in Taiwan.

In this study, age-specific analysis showed that genotype 2a was the most prominent genotype among the 4 age groups, with the highest prevalence in groups aged 20 to 29 years and 30 to 39 years (53.3% and 67.6%, respectively), but there was not a trend between the prevalence of genotypes and age groups. However, in a study by Yu et al,¹³ the authors reported that prevalence of genotype 1b is positively related to age but prevalence of genotype 2a is negatively related to age ($P < 0.01$).

Some limitations of this study need to be addressed. First, the subjects were collected at central Taiwan and were only males. It is not representative of all intravenous drug users in Taiwan. Second, no control population, such as nondrug users, is enrolled to assess whether there is a difference in the distribution of HCV genotypes. Hence, a larger detailed study with subjects collected from other area of Taiwan and including both genders, and drug users and nondrug users is mandatory to resolve these questions.

CONCLUSION

The concordance of antibody to HCV and HCV-RNA is high in selected high-risk groups. HCV genotype 2a is the most prevalent in male intravenous heroin users in central Taiwan, especially in subjects aged 20 to 29 years and 30 to 39 years.

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