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Massive Sero-epidemiological Survey of Hepatitis C Virus: Clustering of Carriers on the Southwest Coast of Tsushima, Japan

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We conducted a mass screening survey for anti-hepatitis C virus antibody (anti-HCV-Ab) among 1,009 inhabitants, 341 males and 668 females, older than 40 years, in south Tsushima in 1989. The overall positive rate for anti-HCV-Ab was 2.3% (2.9% in males and 1.9% in females). The positive rate for anti-HCV-Ab among people with histories of blood transfusions was 14.8% (8/54), which was higher than that (1.6%, 15/955) in people without blood transfusions ($P<0.001$). The positive rate (15.1%, 8/53) in people with an elevated level of glutamic oxalacetic transaminase (GOT, $\geq$41 U/liter) or glutamic pyruvic transaminase (GPT, $\geq$36 U/liter) was significantly higher than that (1.6%, 15/956) for people with normal values of GOT and GPT ($P<0.001$). The most interesting finding was that the anti-HCV-Ab positives without histories of blood transfusions were clustered in a few villages located in the southwestern coastal areas of Tsushima, where the positive rate of 3.7% (13/355) was significantly higher ($P<0.001$) than that of 0.3% (2/600) in other villages.

Key words: Hepatitis C virus — Local clustering

Recently, a non-A, non-B hepatitis virus, termed hepatitis C virus (HCV), was identified molecularly and it became possible to conduct massive sero-epidemiological screenings for viral antibodies to HCV in sera.[1] It has been reported that the prevalence rate of anti-HCV antibody (anti-HCV-Ab) in 2,870 blood donors from the metropolitan area of Tokyo, Japan was just under 1.2%.[2] However, 76% of patients with chronic hepatitis who were free from surface antigen of hepatitis B virus (HBs-Ag) tested positive for anti-HCV-Ab. Among positives for anti-HCV-Ab, half had a history of blood transfusions. In New York,[3] the weighted (adjusted by several risk factors for HCV infection) positive rate for anti-HCV-Ab among blood donors was estimated at 1.4% but the positive rate in those who had an elevated alanine aminotransferase (ALT) level ($\geq$45 U/liter) without anti-HBc-Ab was 7%. In France,[4] less than 1.0% of blood donors were positive for anti-HCV-Ab and more than 5% of those who had an elevated ALT level ($\geq$2 times the normal mean value) were positive for anti-HCV-Ab.

We conducted a mass screening for anti-HCV-Ab among inhabitants of Tsushima Island, located 100 km northwest of the main island of Kyushu. It was revealed that HTLV-I carriers are highly prevalent on Tsushima Island.[5] Blood samples from 1,009 inhabitants, 341 males and 668 females, older than 40 years who voluntarily underwent an annual mass health examination conducted by the local government were collected in 17 villages in south Tsushima in 1989. These serum samples were stored in a deep freezer until examined. The anti-HCV-Ab in sera was tested by the ELISA method using kits provided by Ortho Diagnostic Systems with recombinant antigens from Chiron.[1] ELISA was carried out as recommended by Ortho. Sera were diluted at a ratio of 1:10 and a peroxidase-conjugated monoclonal anti-human IgG was used as the secondary antibody. In all samples, antibodies to both human T lymphotropic virus type I (anti-HTLV-I-Ab) and hepatitis B virus (anti-HBs-Ab) were tested for.

The overall positive rate for anti-HCV-Ab was 2.3% (2.9% in males and 1.9% in females) and it decreased to 1.6% (2.1% in males and 1.3% in females) if people with histories of blood transfusions were excluded (Table I). The positive rate for anti-HCV-Ab was higher in males and in older people (>60 years) than in females and younger people (40–59 years). However, these differences by sex and age group were not statistically significant. The positive rate for anti-HCV-Ab among people with histories of blood transfusions was 14.8% (8/54), which was higher than the 1.6% (15/955) in people without blood transfusions, and this difference was statistically significant ($P<0.001$). In people who had an elevated level of glutamic oxalacetic transaminase (GOT: $\geq$41 U/liter) or glutamic pyruvic transaminase (GPT: $\geq$36 U/liter), the positive rate for anti-HCV-Ab

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Table I. Positive Rates for Anti-HCV Antibody amongst Inhabitants of Tsushima Island Older than 40 Years in 1989

Items compared	Subjects without blood transfusions	All subjects
	Positives/Tested (%)	Positives/Tested (%)
Sex		
Male	7/326 (2.1)	10/341 (2.9)
Female	8/629 (1.3)	13/668 (1.9)
Age		
40–59 years	6/511 (1.2)	9/535 (1.7)
60–	9/444 (2.0)	14/474 (3.0)
Anti-HBs-Ab		
Positive	2/263 (0.8)	5/273 (1.8)
Negative	13/692 (1.9)	18/736 (2.4)
Anti-HTLV-I-Ab[a)]		
Positive	3/215 (1.4)	7/235 (3.0)
Negative	12/689 (1.7)	15/720 (2.1)
Transferase		
GPT≥36 (GOT≥41)	5/46 (10.9)*	8/53 (15.1)*
GPT<35 (GOT<40)	10/909 (1.1)*	15/956 (1.6)*
Transfusions		
Yes	— —	8/54 (14.8)*
No	— —	15/955 (1.6)*

GPT: glutamic pyruvic transaminase. GOT: glutamic oxaloacetic transaminase.
* Differences between groups were statistically significant at $P<0.001$.
a) Fifty-four subjects were excluded because of lack of information.

Table II. Positive Rate for Anti-HCV-Ab among Inhabitants Older than 40 Years in Four Villages Located on the Southwest Coastline and 13 Other Villages on Tsushima Island in 1989

Locality (No. of villages)	Subjects without blood transfusion	All subjects
	Positives/Tested (%)	Positives/Tested (%)
Southwest (4)	13/355 (3.7)*	16/380 (4.2)*
Other (13)	2/600 (0.3)*	7/629 (1.1)*
Total (17)	15/955 (1.6)	23/1009 (2.3)

* Differences between the two groups were statistically significant at $P<0.01$.

was 15.1% (8/53), which was significantly higher ($P<0.001$) than that for people with normal values of GOT and GPT. The positive rates for anti-HCV-Ab in positives and negatives for anti-HBs-Ab were 1.8% (5/273) and 2.4% (18/736), and for anti-HTLV-I-Ab they were 3.0% (7/235) and 2.1% (15/720). The differences between positives and negatives were not statistically significant. The most interesting finding was that most of the anti-HCV-Ab positives without histories of blood transfusions were clustered in a few villages located in the southwestern coastal areas of Tsushima (Table II). There the positive rate was 3.7% (13/355), which was significantly higher ($P<0.001$) than that of 0.3% (2/600) in other villages. The overall positive rate for anti-HCV-Ab among the general population in Tsushima (2.3%) was higher ($P<0.05$) than that in the metropolitan areas of Japan (1.2%). We should compare the positivity rate between two groups after standardizing age distribution, history of blood transfusion and test methods. Nevertheless, we would guess that the value of 3.7% in the general population without blood transfusions in these areas is significantly high. This evidence suggests that HCV has been carried under natural conditions among indigenous people in some HCV-clustering

areas of Japan. From a correlation analysis of the seropositivity between anti-HCV-Ab and anti-HBs-Ab and/or anti-HTLV-I-Ab, the geographical distribution of HCV carriers appeared not to be directly associated with those of HBV and HTLV-I.

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