Original Article

Pilot study for hepatitis virus screening among employees as an effective approach to encourage employees who screened positive to receive medical care in Japan

Aya Sugiyama,1 Toshiko Fujii,1,2 Shintaro Nagashima,1 Masayuki Ohisa,1 Chikako Yamamoto,1 Channarena Chuon,1 Tomoyuki Akita,1 Junko Matsuo,1 Keiko Katayama,1 Kazuaki Takahashi1,3 and Junko Tanaka1

1Department of Epidemiology, Infectious Disease Control and Prevention, Graduate school of Biomedical and Health Sciences, Hiroshima University, and 2Hiroshima Regional Health Medical Promotion Organization, Hiroshima, 3Department of Medical Sciences, Toshiba General Hospital, Tokyo, Japan

Aim: Countermeasures against hepatitis B and C virus (HBV, HCV) infection at work sites in Japan have not yet been implemented. This study aimed to determine the status of viral hepatitis infection among employees in Japan.

Methods: We undertook a workplace-based cross-sectional study from 2011 to 2016 in Hiroshima, Japan. Hepatitis B virus and HCV markers were identified during a routine checkup of employees in 15 enterprises. The screening results were sent to employees directly and not to employers. A thorough examination of the participants who screened positive was encouraged by forwarding to them a referral letter by our research group to specialized medical institutions.

Results: Of the 3015 employees, 2420 (80.3%) underwent hepatitis virus screening. Of these, 13.8% had been screened for hepatitis virus before this survey. The prevalence of hepatitis B surface antigen was 0.95% (n = 23; 95% confidence interval, 0.6–1.3%). The prevalence of hepatitis B core antibody was as high as 31.5% at age 60–69 years, and 41.5% at age 70 years and over. The HCV carrier rate was 0.45% (n = 11; 0.2–0.7%) and 54.5% of them had genotype 2. Thirty-four carriers were detected, and 44.1% of them were detected for the first time; 53.3% of the newly detected carriers visited medical institutions with the referral, and underwent a periodic follow-up or treatment.

Conclusion: Promoting hepatitis virus screening for employees may help detect carriers who are unaware of their infection and require treatment. Submitting the results to employees with a referral letter to medical institutions at the time of positive diagnosis may be effective.

Key words: employees, hepatitis B virus, hepatitis C virus, prevalence, screening

INTRODUCTION

In Japan, the annual number of hepatocellular carcinoma-related deaths has gradually decreased. However, 29,543 people (19,208 men and 10,335 women) died because of malignant liver neoplasms in 2014 (23.6 per 100,000 population).1 In addition, 70–80% of liver cancer cases are caused by chronic hepatitis and cirrhosis due to hepatitis B virus (HBV) or hepatitis C virus (HCV) infection.2

In Japan, approximately 777,000 people are latent hepatitis virus carriers without subjective symptoms.3,4 Therefore, it is important to identify individuals with undiagnosed HBV or HCV infection and implement effective measures to prevent the progression of liver disease.

Although community residents have been provided an opportunity to undergo HBV and HCV screening by the
METHODS

Subjects

This study was undertaken at 15 enterprises in Hiroshima that have outsourced general checkups for their employees to the Hiroshima Regional Health Medical Promotion Organization (Hiroshima, Japan). We selected the 15 enterprises considering the balance of job category, and we first explained the need to for hepatitis virus screening to employers under the same protocol. With the employers’ consent and cooperation, HBV and HCV screening was provided free of charge during general checkups for employees. The 15 enterprises were divided into four categories: customer service enterprises (A, Taxi; B, Taxi; C, Hotel; D, Hotel), industrial enterprises (E, Iron works; F, chemical industry; G, construction industry; H, iron works; I, interior construction industry; J, manufacturing enterprise; K, chemical industry), welfare service enterprises (L, social welfare corporation; M, social welfare corporation; N, social welfare corporation), and education-related enterprises (O, education related) (Table 1). Of the 15 enterprises, 13 were small- and medium-sized enterprises. Two enterprises (F, chemical industry; and J, manufacturing enterprise) were large, and only one branch of each company was investigated.

In total, 2420 consenting participants (1765 men and 654 women aged 18–81 years) were evaluated in this study. The mean age was 47.0 ± 14.4 years; according to the distribution by age group, 0.8% participants were aged ≤19 years, 3.0% were aged ≥70 years, and the proportions of participants in the remaining age groups were evenly distributed. Their ages were adjusted to those in the year 2015 for the calculation of the age-specific prevalence of HBV and HCV.

Research methodology

Questionnaire

A self-administered questionnaire was applied to determine the rate of screening for hepatitis virus infection before this survey, the reasons for a lack of hepatitis virus screening before this survey, the rate of carrier visits to medical institutions, and the awareness of the participants about public funding for hepatitis therapy.

Blood samples and screening

Blood was collected from consenting employees, and hepatitis virus screening was provided free of charge during general checkups for employees at work sites. The results of the testing and general checkups were sent to each employee. The “hepatitis virus screening enrollment card,” which was a reminder (created by our research group) of the hepatitis virus screening date, was also sent to all the participants.

A thorough examination of the participants who screened positive for hepatitis virus infection was encouraged by forwarding the screening results to them together with a referral letter to medical institutions and a list of specialized medical centers that provided hepatitis therapy. In cases in which a participant with a positive diagnosis visited a referral medical institution, the hospital submitted the results of thorough examinations to our research group. Then, we summarized the data about diagnoses and therapeutic measures.

Measurements

Hepatitis virus screening

For HBV screening, hepatitis B surface (HBs) antigen (Architect HBsAg QT; Abbott Japan, Tokyo, Japan), hepatitis B surface antibody (anti-HBs) (Ausab; Abbott Japan), and hepatitis B core antibody (anti-HBc) (Architect HBC-II; Abbott Japan) tests were carried out. In this study, HBV carriers were defined as patients who were positive for HBs antigen.

The method for HCV screening in Japan includes immunnoassays for anti-HCV and the nucleic acid amplification test (NAT) for HCV RNA. First, HCV antibody titers were measured (Lumipulse II Ortho HCV antibody; Ortho-Clinical Diagnostics, Tokyo, Japan). According to the first procedure for HCV screening established by the Ministry of Health, Labour and Welfare of Japan, HCV core antigen testing (Lumipulse Ortho HCV antigen; Ortho-Clinical Diagnostics) was undertaken for participants whose HCV antibody titers were low or moderate. When the HCV core antigen was negative, the NAT was carried out for detecting
| Enterprise                  | Number of employees | Number of participants (%) | M/F    | Age range, years (mean ± SD) | Prevalence, % (95% CI) |
|-----------------------------|---------------------|-----------------------------|--------|-----------------------------|------------------------|
| A Taxi                      | 460                 | 454 (98.7)                  | 434/20 | 25–77 60.5 ± 9.1 1.98 (0.69–3.27) 33.3 (28.4–38.1) 26.2 (21.8–30.6) 2.42 (1.00–3.85) 1.32 (0.27–2.38) |
| B Taxi                      | 150                 | 123 (82.0)                  | 120/3  | 35–68 56.3 ± 7.0 1.63 (0.30–8.37) 21.1 (13.5–28.8) 16.3 (9.4–23.1) 2.44 (0.00–5.18) 1.63 (0.30–3.87) |
| C Hotel                     | 150                 | 107 (71.3)                  | 45/62  | 19–72 37.3 ± 12.2 0.00 (0.00–3.45) 9.4 (3.7–15.0) 12.2 (5.8–18.6) 0.00 (0.00–3.45) 0.00 (0.00–3.45) |
| D Hotel                     | 230                 | 152 (66.1)                  | 102/50 | 21–66 40.7 ± 11.6 0.00 (0.00–1.95) 5.3 (1.7–8.9) 5.9 (2.1–9.7) 0.66 (0.00–1.95) 0.00 (0.00–2.43) |
| **Total of customer service employees (A–D)** | **990**             | **836 (84.4)**              | **701/135** | **19–77 53.0 ± 13.6 1.44 (0.63–2.24) 23.3 (20.3–26.4) 19.3 (16.4–22.1) 1.79 (0.89–2.70) 0.96 (0.30–1.62)** |
| E Iron works                | 80                  | 75 (93.8)                   | 70/5   | 20–81 44.5 ± 16.0 1.33 (0.00–3.94) 20.0 (10.4–29.6) 18.7 (9.4–28.0) 0.00 (0.00–4.92) 0.00 (0.00–4.92) |
| F Chemical industry         | 700                 | 498 (71.1)                  | 440/58 | 19–70 41.7 ± 13.4 0.60 (0.00–1.28) 12.1 (9.1–15.0) 8.8 (6.3–11.4) 0.40 (0.00–0.96) 0.20 (0.00–0.59) |
| G Construction industry     | 100                 | 97 (97.0)                   | 92/5   | 21–71 45.6 ± 14.1 1.03 (0.00–3.05) 14.4 (7.2–21.7) 12.4 (5.6–19.2) 0.00 (0.00–3.80) 0.00 (0.00–3.80) |
| H Iron works                | 100                 | 69 (69.0)                   | 52/17  | 19–63 42.2 ± 11.6 0.00 (0.00–5.35) 8.7 (1.9–15.5) 10.1 (2.8–17.5) 2.9 (0.00–6.89) 0.00 (0.00–5.35) |
| I Interior construction industry | 100               | 62 (62.0)                   | 17/26  | 21–72 46.2 ± 12.8 1.61 (0.00–4.76) 8.1 (1.1–15.0) 6.5 (0.2–12.7) 0.00 (0.00–5.95) 0.00 (0.00–5.95) |
| J Manufacturing industry    | 60                  | 56 (93.3)                   | 7/49   | 26–63 46.9 ± 9.0 0.00 (0.00–6.59) 7.1 (3.1–14.0) 8.9 (1.3–16.6) 0.00 (0.00–6.59) 0.00 (0.00–5.95) |
| K Chemical industry         | 120                 | 66 (55.0)                   | 56/10  | 20–72 40.3 ± 12.6 0.00 (0.00–5.59) 7.6 (1.1–14.1) 9.1 (2.0–16.2) 1.52 (0.00–4.47) 0.00 (0.00–5.59) |
| **Total of industrial employees (E–K)** | **1260**            | **923 (73.3)**              | **753/170** | **19–81 42.5 ± 13.4 0.65 (0.13–1.17) 11.8 (9.7–14.0) 10.0 (8.0–12.0) 0.54 (0.07–1.02) 0.11 (0.00–0.32)** |
| L Social welfare corporation | 120                 | 72 (60.0)                   | 21/51  | 20–70 39.2 ± 15.0 0.00 (0.00–5.12) 4.2 (0.0–8.8) 6.9 (0.96–12.9) 1.39 (0.00–4.10) 1.39 (0.00–4.10) |
| M Social welfare corporation | 400                 | 396 (99.0)                  | 254/142| 18–80 45.0 ± 15.0 1.01 (0.02–2.00) 11.6 (8.4–14.9) 14.4 (10.8–18.0) 0.51 (0.00–1.20) 0.00 (0.00–0.93) |
| N Social welfare corporation | 79                  | 58 (73.4)                   | 21/37  | 23–69 48.8 ± 12.4 1.72 (0.00–5.09) 8.6 (1.2–16.0) 6.9 (0.3–13.5) 0.00 (0.00–6.36) 0.00 (0.00–6.36) |
| **Total of welfare service employees (L–N)** | **599**             | **526 (87.8)**              | **296/230** | **18–80 44.6 ± 14.9 0.95 (0.12–1.78) 10.3 (7.6–12.9) 12.6 (9.6–15.5) 0.57 (0.00–1.21) 0.19 (0.00–0.56)** |
| O Education-related         | 166                 | 135 (81.3)                  | 15/119 | 17–74 49.1 ± 11.0 0.00 (0.00–2.73) 6.7 (2.4–11.0) 8.2 (3.4–12.9) 1.48 (0.00–3.53) 0.74 (0.00–2.19) |
| **Total (A–O)**             | **3015**            | **2420 (80.3)**             | **1765/654** | **18–81 47.0 ± 14.4 0.95 (0.56–1.34) 15.2 (13.7–16.7) 13.6 (12.2–15.1) 1.03 (0.63–1.44) 0.45 (0.19–0.72)** |
HCV RNA (COBAS TaqMan HCV Auto; Roche Diagnostics, Tokyo, Japan). However, based on the revisions to the first procedure for HCV screening proposed by the Ministry of Health, Labour and Welfare in 2013, HCV core antigen testing was not used after 2013. Therefore, NAT was undertaken for participants whose HCV antibody titers were moderate or low.

Genotyping of HBV DNA and HCV RNA
For HBs antigen-positive cases, the HBV genotype was determined using the direct sequencing method and the S gene region primer.

For HCV carriers, the HCV genotype was determined using the direct sequencing method and the core region primer.

Analysis of HBV phylogenetic trees
For the analysis of the HBV phylogenetic trees, multiple sequence alignment was carried out using CLUSTALW, and unrooted phylogenetic trees were constructed using the neighbor-joining method. The phylogenetic tree was then displayed using the genetic tree system.

Statistical analyses
Statistical analyses were carried out with JMP version 11 (SAS Institute, Cary, NC, USA).

A χ²-test was used to compare categorical data. A multivariate logistic regression analysis model was used to assess the relative contributions of age, gender, and job categories on the prevalence of HBV and HCV infections. P-values less than 0.05 were considered significant.

Ethical considerations
This study was approved by the Research Ethics Committee of Hiroshima University (Hiroshima, Japan; approval number: Eki620–3). All participants signed a written informed consent.

RESULTS
Rate of screening and level of awareness of hepatitis virus infection
Of the 3015 employees from the 15 enterprises, 2420 (80.3%) agreed to undergo hepatitis virus screening (Table 1). Although we offered all employees to participate in this survey under the same protocol, the examinees rate was significantly different by type of enterprise (55–99%, P < 0.0001). The rate was also significantly different between the four job categories: 84.4% in customer service enterprises, 73.3% in industrial enterprises, 87.3% in welfare service enterprises, and 81.3% in an education-related enterprise (P < 0.0001).

Of the 2420 participants, 335 (13.8%; 95% confidence interval [CI], 11.1–15.7%) had been screened for hepatitis virus before this survey. Of the remaining 2072 participants, 36.2% had no opportunity to be tested, 34.8% did not know about the existence of hepatitis virus screening, and 16.1% thought that hepatitis virus screening was not necessary.

Among the 2420 participants, only 13.2% had knowledge of the treatment of viral hepatitis, and only 9.7% knew about the public funding for HBV/HCV treatment.

Prevalence of HBV and HCV infection
The prevalence of HBV infection determined by HBsAg positivity was 0.95% (n = 23 [20 men and 3 women]; 95% CI, 0.6–1.3%), 1.76% among those aged 40–49 years, and 2.34% among those aged >70 years (Fig. 1).

Anti-HBc was present in 15.2% (95% CI, 13.7–16.7%) of the participants, and anti-HBs was present in 13.6% (95% CI, 12.2–15.1%) of cases. A higher percentage of the participants in the older age groups had anti-HBc: 31.5% (95% CI, 27.3–35.6%) of those aged 60–69 years and 41.5% (95% CI, 32.9–50.1%) of those aged 70–79 years. Anti-HBs was also common in elderly groups (Fig. 1b,c).

Of the 2420 participants, 9 (0.37%) participants had high anti-HCV titers and 16 (0.66%) participants had low or medium anti-HCV titers, totaling 25 (1.03%; 95% CI, 0.6–1.4%) participants positive for anti-HCV. The remaining 2395 (98.97%) participants were anti-HCV negative (Fig. 2).

All 9 participants with high anti-HCV titers were positive in the NAT. Of the 16 participants with low or medium anti-HCV titers, 2 were positive and 14 were negative in the NAT. Therefore, of the 25 anti-HCV-positive participants, 11 (9 men and 2 women) were HCV carriers (prevalence, 0.45%; 95% CI, 0.2–0.7%). By age group, 0.43% of those aged 50–59 years and 1.54% of those aged 60–69 years were HCV carriers. None of the participants aged <50 years or ≥70 years were HCV carriers (Fig. 1d,e).

The prevalence of HBV and HCV infection in the four job categories adjusted for age and sex was not significantly different.

Genotyping of HBV or HCV carriers
Among the 23 HBV carriers who were diagnosed, the majority had genotype C (n = 19, 82.6%). Genotypes A and B were present in one participant each. Genotype A
was found in a woman aged 47 years. The genotype of the remaining two HBV carriers could not be determined.

However, among the 11 HCV carriers, HCV genotype 1b was present in 5 participants (45.5%; age range, 57–63 years), whereas genotype 2 was present in 6 participants (54.5%; age range, 49–63 years). For genotype 2, genotype 2a was present in 2 HCV carriers and genotype 2b was present in 4 HCV carriers.

**Phylogenetic analysis of HBV carriers**

Among the 23 HBV carriers, 19 genomes were studied by phylogenetic analysis. Of these, 17 genomes were genotype C2, 1 was genotype A1, and 1 was genotype B1 (Fig. 3). Most of the genomes that belonged to genotype C2 were closely related to Japanese or Chinese isolates; however, one genome (S8-N11–7206) was similar to the Taiwan isolate, with a degree of similarity of 99.6%. The HBV A1 isolate (S12-N12–7111) was homologous to the Indian isolate, with a degree of similarity of 99.2%, and the HBV B1 isolate (S1-N11–6240) was homologous to the Japanese isolate, with a degree of similarity of 99.0%.

**Comparison of HBV infection status by birth year**

A comparison between participants born before 1986, when a national immunoprophylactic vaccination program for babies born to HBV carrier mothers started in Japan (n = 2012), and participants born after 1986 (n = 273) indicated that the proportion of HBV carriers in these two groups was 1.1% and 0.0%, respectively. The percentage of participants with a previous infection was 16.5% and 1.1%, respectively, and the proportion of participants who had never been infected was 80.4% and 94.1%, respectively (P < 0.0001, χ²-test; Table 2). Similar results were found for men and women.

**Diagnosis of hepatitis virus carriers**

Of the 2420 participants, 34 participants were hepatitis virus carriers (23 HBV carriers and 11 HCV carriers). The results of the questionnaire indicated that, of the 34 carriers, 44.1% (10 HBV carriers and 5 HCV carriers) were diagnosed for the first time (Fig. 4). Three HBV carriers (9%) had never visited a medical institution despite the knowledge of their infection. Four HBV carriers and two HCV carriers (18%) were under treatment. Three HBV
carriers and one HCV 1212carrier (12%) answered that they were already cured.

**Encouragement to visit medical institutions with a referral letter and feedback from these institutions**

A letter of referral to medical institutions was sent to each of the 23 HBV carriers and 11 HCV carriers who were diagnosed during the study period, to encourage a visit to a medical institution. By 31 December 2016, the medical centers had submitted the results of thorough examinations of 16 HBV carriers (69.6%) and 3 HCV carriers (27.3%) to our research group.

Among the 15 hepatitis virus carriers who were diagnosed for the first time (10 HBV carriers and 5 HCV carriers), 8 carriers (53.3%, 7 HBV carriers and 1 HCV carrier) visited a referral medical institution (Table 3). The rate of visiting a medical institution was different between HBV carriers and HCV carriers who were diagnosed for the first time (HBV, 80%; HCV, 20%; \( P < 0.0253 \)). The feedback from the medical institutions revealed that, among the 8 detected carriers, 6 were asymptomatic and 2 presented with chronic hepatitis, including 1 HBV carrier for whom cancer in organs other than the liver was detected by chance during the visit to the medical institution. All carriers were instructed to undergo a periodic follow-up. These carriers had not undergone hepatitis virus screening before this survey because of the lack of opportunity or knowledge. Only 1 HCV carrier knew about the treatment of viral hepatitis infection and the financial support system for hepatitis therapy.

Thirteen HBV carriers and 6 HCV carriers had undergone a hepatitis virus screening test before this survey (Table 4). Three HBV carriers had never visited a medical institution despite knowledge of their infection because they thought there was no need or opportunity. However, these 3 HBV carriers attended a referral medical institution, and 2 of them were instructed to undergo periodic follow-up. Two of the 3 HBV carriers who answered they were already cured visited a referral medical institution and both of them were diagnosed as asymptomatic carriers and were instructed to undergo periodic follow-up.

Among the 13 HBV carriers who had undergone a hepatitis virus screening test before this survey, 6 (46.2%) had knowledge about the treatment of viral hepatitis and only 1 (7.7%) was aware of the financial support system for HBV/HCV treatment. However, all 6 HCV carriers knew

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about the treatment and 5 of them (83.3%) knew about the public funding for HBV/HCV treatment.

DISCUSSION

IN THIS STUDY involving employees (n = 2420) in Hiroshima between 2011 and 2016, the screening rate for hepatitis virus infection before this study was 13.8% (95% CI, 11.1–15.7%). Compared with the rate of screening for hepatitis virus infection of 7.2% (95% CI, 3.3–11.2%) in our previous pilot study in 2008, also carried out among employees in Hiroshima, the screening rate at work sites seems to have increased. However, the reported screening rate was 33.6% (95%
CI, 32–35%) in the general population in the Hiroshima Prefecture\(^7\) and 17.8% in a nationwide survey.\(^8,9\) As in a previous report,\(^10\) this study suggested the screening rate at work sites is still low compared with that in the general population.

The questionnaire results indicated that the reasons for the low rates of hepatitis virus screening before this survey were “lack of opportunity for screening” (36.2%) and “lack of knowledge of the existence of screening” (34.8%). Our study provided both information and opportunity for hepatitis virus screening. As a result, approximately 80% of employees were willing to undergo screening. Despite offering the same protocol, the examinees’ rate was significantly different among the 15 enterprises as well as among the four job categories. These results suggest that the interest in hepatitis virus screening might differ depending on each enterprise or job type.

It is desirable to set up screening programs at the same chance of general checkups conducted by each company. Employers should undertake the necessary measures for carriers to protect privacy. Therefore it is recommended to return the result of hepatitis virus test to employees, not to employers. In this study, the screening results were sent directly to employees and not to employers.

Of the 2420 participants, 23 HBV carriers and 11 HCV carriers were diagnosed in this study. Furthermore, 44.1% of the carriers (10 HBV carriers and 5 HCV carriers) were informed of their infection for the first time by the screening provided in this study. The rate of visits to medical institutions after the detection of HBV or HCV infection while screening the general population was reported to be 66.2%.\(^8,9\) In this study, visits to medical institutions by the participants who screened positive were encouraged by sending them a letter of referral to medical institutions and a list of specialized medical centers providing hepatitis therapy. Among the newly detected 15 carriers, 8 carriers visited these referral institutions and each carrier underwent a periodic follow-up. Although the number of subjects was small, there was a significant difference in the rates of visiting medical institutions with the referral letter between HBV carriers and HCV carriers who were detected for the first time (HBV, 80%; HCV, 20%). We could not clarify the reason for the difference, but further improvement may be necessary in terms of the method of positive notification.

In this study, not only the newly detected carriers but also carriers who had never visited a medical institution despite knowledge of their infection, and those who did not know they were not cured, attended a referral medical center. These findings suggest that the submission of the screening results to employees but not employers, and

| Table 2 Summary of hepatitis B virus (HBV) markers among employees screened for hepatitis infection in Hiroshima, grouped by birth year |
| --- |
| **Status** | **HBV carrier** | **Total** | **Anti-HBc** | **Anti-HBs** |
| **Total** | **Before 1985** | **After 1986** | **Before 1985** | **After 1986** |
| **Men** | | | | |
| **Total** | | | | |
| **Women** | | | | |
| **Total** | | | | |
| **Birth year** | | | | |
| **Before 1985** | | | | |
| **After 1986** | | | | |
| **HBV carrier, total** | | | | |
| **n (%)** | | | | |
| **Previous infection, total** | | | | |
| **Not infected, total** | | | | |
| **Total** | | | | |
| **HBV infection status was significantly different between those born before 1986 and after 1986 (χ^2-test).** |

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enclosing a letter of referral to medical institutions and a list of specialized medical centers at the time of positive diagnosis, might be effective for promoting medical care. However, many individuals forget that they underwent screening previously and sometimes incorrectly interpret the screening results. For this reason, we sent the “hepatitis virus screening enrollment card” to all participants to help them remember the screening date. The card has also been effectively used in the administrative service of Hiroshima prefecture and some medical facilities.

Of the total participants, only 13.8% were aware of the treatment of viral hepatitis, and only 9.3% knew about public funding for hepatitis treatment. Among the HCV carriers who were aware of their infection before this study, most of them also knew about treatment and public funding. In turn, some HBV carriers knew about treatment but only a few knew about public funding. Therefore, further measures aimed at improving awareness of treatment and public financial support for viral hepatitis should be taken.

To the best of our knowledge, no research has been reported to estimate the prevalence of HBV and HCV carriers based on serological surveys of the large-scale employment population in Japan. We evaluated the prevalence of HBV and HCV carriers as well as the prevalence of anti-HBc, HBV DNA genotyping, HCV RNA genotyping, and HBV phylogenetic trees. As a result, the overall prevalence of HBV carriers (HBsAg positive) and HCV carriers was 0.95% (95% CI, 0.56–1.34%) and 0.45% (95% CI, 0.19–0.72%), respectively, among employees. Compared with the general population in Japan, the overall prevalence of HBsAg and anti-HCV was reported to be 0.31%, and 0.26%, respectively, based on data for first-time blood donors. The prevalence of HBV and HCV carriers in the workplace population tended to be higher than that in first-time blood donors, who are considered to represent a healthy population. Individuals with known HBV or HCV infection cannot donate blood in Japan. Therefore, first-time blood donors represent a cohort that is not aware of hepatitis viral infections. In contrast, this study included participants who had been screened previously. This fact may help explain the discrepancies in the prevalence between our study cohort and first-time blood donors. In addition, another explanation may be the low screening rates at work sites. Unlike the results from the first-time blood donors, the prevalence of HBsAg in participants aged in their 40s was high and the prevalence of HCV carriers older than 70 years was low in this study. These differences may be due to the relatively low number of each age group in this study.

The prevalence of anti-HBc was as high as 31.5% at age 60–69 years and 41.5% at age ≥70 years. These results suggest that older age groups have a greater risk of HBV reactivation. With regard to HBV genotypes in Japan, approximately 30% are genotype B, and approximately 60% are genotype C. Genotype A, which has a high probability of becoming chronic and causing horizontal transmission, has tended to increase slightly over the past few years. For the 23 identified HBV carriers in this study, approximately 80% were genotype C, and only 1 HBV carrier was genotype A. The phylogenetic analysis revealed that the only genotype A carrier had genotype A1, which originated in Asia, not in the USA or Europe.
Table 3 Characteristics of hepatitis B virus (HBV) and hepatitis C virus (HCV) carriers who were diagnosed for the first time during this survey of hepatitis infection among employees in Hiroshima

| Age, years | Sex | Enterprise        | Visited medical institution with the referral letter of this study | Diagnosis | Outcome                        | Reason why no hepatitis virus screening test done before this survey | Knowledge about treatment for viral hepatitis | Knowledge of financial support from government for HBV/HCV treatment |
|-----------|-----|-------------------|-------------------------------------------------------------|-----------|--------------------------------|------------------------------------------------------------------|-----------------------------------------------|-------------------------------------------------------------|
|           |     |                   |                                                              |           |                                |                                                                 |                                               |                                                             |
| HBV       | 77  | M                 | A, Taxi                                                      | Yes       | Asymptomatic carrier          | Periodic follow-up                                               | Lack of knowledge                              | No                                                          |
| (n = 10)  | 69  | M                 | A, Taxi                                                      | Yes       | Asymptomatic carrier          | Detected cancer in organs other than the liver                   | Lack of knowledge                              | No                                                          |
|           | 64  | M                 | B, Taxi                                                      | Yes       | Asymptomatic carrier          | Periodic follow-up                                               | No opportunity                                | No                                                          |
|           | 46  | F                 | D, Hotel                                                     | Yes       | Asymptomatic carrier          | Periodic follow-up                                               | No opportunity                                | No                                                          |
|           | 37  | M                 | E, Chemical industry                                        | Yes       | Asymptomatic carrier          | Periodic follow-up                                               | No opportunity                                | No                                                          |
|           | 55  | M                 | A, Taxi                                                      | Yes       | Chronic hepatitis             | Periodic follow-up                                               | No answer                                     | No                                                          |
|           | 39  | M                 | A, Taxi                                                      | Yes       | Chronic hepatitis             | Periodic follow-up                                               | No opportunity                                | No                                                          |
|           | 69  | M                 | A, Taxi                                                      | No        |                               |                                                                  | No answer                                     | No                                                          |
|           | 59  | M                 | B, Taxi                                                      | No        |                               |                                                                  | Lack of knowledge                             | No                                                          |
|           | 59  | F                 | N, Social welfare                                           | No        |                               |                                                                  | No opportunity                                | No                                                          |
|           | 57  | M                 | E, Chemical industry                                        | Yes       | Asymptomatic carrier          | Periodic follow-up                                               | Lack of knowledge                             | No                                                          |
| HCV       | 49  | M                 | A, Taxi                                                      | No        |                               |                                                                  | No answer                                     | Yes                                                         |
| (n = 5)   | 61  | M                 | A, Taxi                                                      | No        |                               |                                                                  | Unnecessary                                   | No                                                          |
|           | 63  | M                 | A, Taxi                                                      | No        |                               |                                                                  | No opportunity                                | No                                                          |
|           | 62  | F                 | O, Education-related                                        | No        |                               |                                                                  | No opportunity                                | No                                                          |

–, Unknown. F, female; M, male.
| Medical care for hepatitis virus infection before this survey | Age, years | Sex | Enterprise | Visited medical institution with referral letter from this study | Diagnosis | Outcome | Knowledge of financial support from government for HBV/HCV treatment | Knowledge about the treatment for viral hepatitis |
|-------------------------------------------------------------|-----------|-----|------------|---------------------------------------------------------------|-----------|---------|------------------------------------------------------------------|-------------------------------------------------|
| **HBV** (*n* = 13)                                          |           |     |            |                                                               |           |         |                                                                  |                                                 |
| Never visited                                              | 57        | M    | A, Taxi    | Yes                                                           | Asymptomatic carrier | No follow-up | No                                                        | No                                              |
| a medical institution before this study                    | 63        | M    | A, Taxi    | Yes                                                           | Asymptomatic carrier | Periodic follow-up | Yes                                                      | No                                              |
| Under treatment                                            | 46        | M    | G, Construction industry | Yes                                           | Asymptomatic carrier | Periodic follow-up | No                                                        | No                                              |
| Cured                                                      | 42        | M    | M, Social welfare | Yes                                                   | Asymptomatic carrier | Periodic follow-up | No                                                        | No                                              |
| Under treatment                                            | 42        | M    | E, Iron works | No                                                        | –               | –         | No                                                        | No                                              |
| Cured                                                      | 34        | M    | E, Chemical industry | No                                                       | –               | –         | Yes                                                      | No                                              |
| Cured                                                      | 37        | M    | M, Social welfare | No                                                       | –               | –         | Yes                                                      | Yes                                             |
| Cured                                                      | 67        | M    | A, Taxi    | Yes                                                           | Asymptomatic carrier | Periodic follow-up | No                                                        | No                                              |
| Cured                                                      | 46        | M    | F, Chemical industry | Yes                                                   | Asymptomatic carrier | Periodic follow-up | Yes                                                      | No                                              |
| Cured                                                      | 35        | M    | M, Social welfare | No                                                       | –               | –         | No                                                        | No                                              |
| Unknown                                                    | 61        | M    | A, Taxi    | Yes                                                           | Asymptomatic carrier | No follow-up | Yes                                                      | No                                              |
| Cured                                                      | 47        | M    | L, Interior construction industry | Yes                                           | Asymptomatic carrier | Periodic follow-up | Yes                                                      | No                                              |
| Unknown                                                    | 45        | F    | M, Social welfare | Yes                                                   | Chronic hepatitis | Periodic follow-up | No                                                        | No                                              |
| **HCV** (*n* = 6)                                           |           |     |            |                                                               |           |         |                                                                  |                                                 |
| Under treatment                                            | 59        | M    | A, Taxi    | No                                                        | –               | –         | Yes                                                        | Yes                                             |
| Cured                                                      | 60        | M    | B, Taxi    | No                                                        | –               | –         | Yes                                                        | Yes                                             |
| Unknown                                                    | 52        | F    | L, Social welfare | Yes                                                   | Chronic hepatitis | Therapeutic interventions | Yes                                                      | No                                              |
| Cured                                                      | 57        | M    | B, Taxi    | Yes                                                           | Cirrhosis and liver cancer | Already receiving treatment | Yes                                                      | Yes                                             |
| Unknown                                                    | 57        | M    | A, Taxi    | No                                                        | –               | –         | Yes                                                        | Yes                                             |

--, Unknown; F, female; M, male.
For HCV, genotype 1b is believed to be the most common genotype in Japan, accounting for approximately 70% of cases. In addition, genotypes 2a and 2b are present in approximately 20% and 10% of cases, respectively. Although we detected only 11 HCV carriers in this study, 54.5% of the carriers had genotype 2. Recently, it has been reported that the proportion of participants with genotype 2 tended to be higher in younger age groups,\textsuperscript{7,16} a similar result was shown in this study.

In addition, as serological data for large-scale general populations is valuable, we also evaluated the effectiveness of preventive actions against mother-to-child transmission implemented from 1986 in Japan, and as a result, no HBV carriers were identified among employees born after 1986.

CONCLUSION

A 6-YEAR HEPATITIS virus infection study was carried out with 2420 employees in 15 enterprises. The results indicated that the screening rate for hepatitis virus infection is still low at work sites. Hepatitis virus screening and visits to medical institutions after screening were promoted by forwarding the screening results to employees but not to employers. Enclosing a letter of referral to medical institutions and a list of specialized medical centers at the time of positive diagnosis may also be effective. Furthermore, information about hepatitis virus infection, including treatment and the financial support system for hepatitis treatment, needs to be provided at work sites.

ACKNOWLEDGMENTS

THIS WORK WAS undertaken as a part of the Research on Hepatitis for the Ministry of Health, Labour and Welfare, Japan and was supported by grants from the Ministry of Health, Labour and Welfare, Japan (H22-kanen-ippan-012, H25-kanen-ippan-010, and H28-kansei-ippan-001).

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