# **Ongoing Care and Follow-up Behavior of Working Age Japanese with Hepatitis C Virus**

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**Abstract:** <u>Background</u>: Persons infected with HCV (Hepatitis C Virus) may not actively seek medical attention as they are often asymptomatic for long periods of time. <u>Objective</u>: The aim of this study was to investigate ongoing care and follow-up behaviors of working age Japanese who are currently infected with HCV. <u>Methodology</u>: We recruited a total of 156 persons aged 20-69 years (78 male and 78 female) who had been infected with HCV and were registered with an internet survey company. These individuals were asked to answer an anonymous questionnaire which focused on how they had found out about being infected with HCV, if they had received any specific treatment, their frequency of visits to medical facilities, and if they had received prior medication. <u>Results</u>: Of the 156 participants 35.9% reported havd no prior treatment at all, while 30.1% had no regular visits to medical facilities regarding their condition. The main reason for not visiting medical facilities was the lack of doctor's recommendation in 19.0% of men and in 31.4% of women respondents with HCV infection. Those who had never received any treatment were most likely to be in their 30s (55.6%). <u>Conclusion</u>: This study suggests that a considerable number of HCV carriers have never received treatment for HCV infection. Currently in Japan, systems appear to be lacking which might prompt HCV positive individuals to visit hepatology specialists and obtain appropriate treatment.

Keywords: Care, carrier, hepatitis C, Japan, working.

# **INTRODUCTION**

Progression of viral hepatitis to liver cirrhosis and even liver cancer can often be prevented by appropriate treatment, especially if the infection is identified at an early stage [1, 2]. In Japan, the Basic Act on Hepatitis Measures was enacted in 2009 and has been supporting and promoting a project to provide opportunities for viral hepatitis screening [3]. Although it is important for persons with HCV infection to receive continuous treatment [4], such individuals may not be motivated to do so because they are often asymptomatic for a long period of time [5]. However, as a result of recent improvements in the treatment of HCV infection, the therapeutic scope has expanded to include carriers who were not previously targeted for treatment [6]. Effective treatments were generally lacking in the past for persons infected with HCV and some prejudice against these people may also exist [7].

At a practical level, HCV carriers also need to undergo follow-up treatment such as abdominal ultrasonography once every 4-6 months and hematological examination once every 2 months for managing hepatocellular carcinoma, even when the alanine aminotransferase level is <80 IU/l, in accordance with current guidelines [8]. Carriers of working age are an important target of early-phase treatment, and it is also necessary to detect hepatic cirrhosis and cancer at an early stage in this population [9]. Despite these facts however, it remains unclear exactly what proportion of the Japanese working population has already undergone testing. The aim of this study was, therefore, to investigate ongoing care and follow-up behaviors of working age Japanese who are currently infected with HCV.

## **METHODS**

#### **Recruitment of Participants**

Nineteen thousand and four hundred Japanese people of working age (20-69 years) who had agreed to respond to various health-related issues were randomly extracted from the registry of an internet research company in September 2012. All participants who were interested in taking part in the survey had initially been offered a financial incentive to respond and had voluntarily registered with the survey company. From this group, persons who had been previously infected with HCV were identified as follows. Firstly, a letter was sent to HCV-infected persons asking if they had undergone treatment for various diseases such as type 1 and 2 diabetes, hyperuricemia, hypercholesterolemia, hepatitis B, hepatitis C, or chronic renal failure to ensure that the survey was aimed at identifying HCV cases. After the survey company had identified 138 male and 156 female individuals with HCV infection, an additional letter was sent to them which included questions designed for the present study. Although the questionnaire was anonymous, respondents were required to consent to the results being published in academic journals. The web survey company ceased recruitment when the total number of participants reached the target number. Participants were recruited in clusters, target-

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ing 75 individuals of each sex for HCV infection, giving a total of 150 respondents in the first instance.

#### Questionnaire

The questionnaire utilized in this study was anonymous. Participants were asked their age and occupation (company employee, self-employed, or part-time), and were then requested to choose one of the following categories pertaining to how they had found out about being infected with HCV. The answer choices were as follows: (1) at a regular health check-up; (2) at the time of pregnancy health screening or pre-surgical screening in a hospital; (3) at a visit to a medical facility because of ill health; (4) at the time of blood donation; (5) at a visit to a medical facility prompted by anxiety regarding blood transfusion or the use of blood products in the past; and (6) other reasons. Participants were asked if they had received any specific treatment for HCV. Participants were also requested to select an answer from the following regarding the frequency of visits to medical facilities for HCV infection in the previous year: (1) at least once a week; (2) about once a month; (3) about once every 3 months; (4) about once every 6 months; (5) about once a year; or (6) no periodic visits. Participants who reported that they had received no prior medications for their infection were asked to give reasons by choosing at least one of the following: (1) there were no subjective symptoms; (2) my doctor did not recommend it; (3) bothersome; (4) too busy working; (5) financially difficult; (6) completely cured; or (7) anxious about work colleagues finding out about my infection status / did not want anyone at work to know.

#### **Statistical Analysis**

The proportion of respondents who were receiving and not receiving any form of treatment or follow-up from physicians for HCV infection was ascertained. We then identified the characteristics of persons who had not been treated for HCV infection by cross tabulation. For each calculation the 95% confidence interval was calculated, with IBM SPSS Statistics version 20 was used for all statistical analyses.

## Ethics

This study was approved by the Kitasato University School of Medicine Ethics Committee prior to implementation. We obtained a written informed consent for participation in this study from each respondent.

#### RESULTS

Completed responses to the questionnaire were obtained from 156 individuals for who their characteristics are shown on Table **1**. A total of 156 persons who had been diagnosed with HCV were extracted to obtain a male-to-female ratio of 1:1. Respondents in their 50s accounted for the largest proportion of both genders; while for occupation, company employees were the most common in both genders. HCV infection was discovered during a regular health check-up in 29.5% and during a visit to a medical facility because of ill health in 28.2% of cases. Infection was discovered at the time of blood donation among 14.1% of HCV carriers. There was a history of no prior treatment for HCV infection reported by 35.9% of HCV carriers, with 30.1% of HCVinfected individuals reporting no periodic visits. Table **2** indicates the percentages for prior treatment, frequency of visits to medical facilities in the previous year, and reasons for not visiting medical facilities for HCV infection, stratified by gender. The proportion of individuals reporting no prior treatment was higher among women (44.9%) than men (26.9%). With regard to the frequency of visits to medical facilities, no regular visits were reported by 29.5% of men and 30.8% of women with HCV infection. The main reasons for not visiting were that the illness had been cured (61.9% of men), and the lack of a doctor's recommendation to visit a medical facility (31.4% of women).

Table 1. Participant characteristics.

	Ν	(%)*
Gender		
Male	78	(50.0)
Female	78	(50.0)
Age (yrs)		
20-29	4	(2.6)
30-39	18	(11.5)
40-49	45	(28.8)
50-59	59	(37.8)
60-69	30	(19.2)
Occupation		
Company employee	80	(51.3)
Self-employed	32	(20.5)
Part-time	44	(28.2)
HCV Infection Status Discovery		
At a regular health check-up	46	(29.5)
At the time of pregnancy health screening or pre-surgical screening	34	(21.8)
At a visit to a medical facility due to ill health	44	(28.2)
At the time of blood donation	22	(14.1)
At a visit to a medical facility prompted by anxiety regarding blood transfusion or the use of blood products in the past	9	(5.8)
Other Reason	5	(3.2)
Prior Treatment for HCV Infection		
Yes	100	(64.1)
No	56	(35.9)
Frequency of Visits to Medical Facilities		
At least once a week	8	(5.1)
About once a month	26	(16.7)
About once every three months	32	(20.5)
About once every six months	17	(10.9)
About once a year	26	(16.7)
No periodic visits	47	(30.1)

\*N=156

	Male		Female			
	%	(95%CI)*	%	(95%CI)*		
Prior Treatment for HCV Infection						
Yes	73.1	(63.2-82.9)	55.1	(44.1-66.2)		
No	26.9	(17.1-36.8)	44.9	(33.8-55.9)		
Fr	equency of Visits to Me	dical Facilities				
At least once a week	5.1	(0.2-10.0)	5.1	(0.2-10.0)		
About once a month	21.8	(12.6-31.0)	11.5	(4.4-18.6)		
About once every three months	20.5	(11.6-29.5)	20.5	(11.6-29.5)		
About once every six months	10.3	(3.5-17.0)	11.5	(4.4-18.6)		
About once a year	12.8	(5.4-20.2)	20.5	(11.6-29.5)		
No periodic visits	29.5	(19.4-39.6)	30.8	(20.5-41.0)		
Reason for not Visiting Medical Facilities	(n=21)		(n=35)			
No subjective symptoms	14.3	(0-29.3)	28.6	(13.6-43.5)		
My doctor did not recommend it	19.0	(2.3-35.8)	31.4	(16.0-46.8)		
Bothersome	0.0	-	14.3	(2.7-25.9)		
Too busy working	9.5	(0-22.1)	5.7	(0-13.4)		
Financially difficult	19.0	(2.3-35.8)	5.7	(0-13.4)		
Completely cured	61.9	(41.1-82.7)	8.6	(0-17.8)		
Anxious about what other people will think / did not want anyone at work to know	0.0	-	0.0	-		

Table 2. Prior treatment for hepatitis C virus (HCV) infection.

\*95% Confidence Intervals

Table **3** indicates the proportion of respondents with HCV infection who had not received any prior treatment. Those without prior treatment were most frequently in their 30s (55.6%), while part-time workers without prior treatment accounted for 40.9% of those with HCV infection. Based on when the infection had been detected, 44.4% of their detections occurred at a visit to a medical facility prompted by anxiety regarding blood transfusion or use of blood products in the past, with further 41.2% occurring at the time of health screening for pregnancy or pre-surgical screening in a hospital.

# DISCUSSION

Overall, this study suggests that a considerable proportion of working-age Japanese people have not received treatment or follow-up for HCV infection, with HCV carriers most likely to seek treatment only when deterioration of their physical condition prompted a visit to medical facilities. Furthermore, detection of their infection did not necessarily lead to treatment when discovered at the time of blood donation, pregnancy or pre-surgical health screening in a hospital which did not have a direct link for specialists of hepatology. The gap between screening opportunities and post-diagnosis care of HCV infection needs to be addressed [10]. Infection with HCV was most frequently detected when the carrier visited a medical facility because of ill health, and the lack of prior treatment for viral hepatitis was less frequent among these carriers when compared to others. Although it is unclear whether the ill health suffered by participants in the current study was attributable to HCV infection; in research from the United States a similar proportion of HCV-infected persons were identified due to liver related symptoms [11]. Where HCV status was discovered during blood donation, blood sampling during pregnancy or screening prior to surgery; the lack of treatment which was slightly more common among HCV carriers suggests a general failure in referring these individuals to appropriate specialists. As such, it is clearly necessary to emphasize post-test counseling for those with positive results and to establish more effective linkage to follow-up care and treatment by appropriate hepatology specialists [12].

In the current study, a lack of prior treatment was more frequent among female than male HCV carriers, which is similar to a previous study of HCV-infected patients conducted in the United States [13]. In addition, it was suggested that population groups that were more likely not to receive treatment included those aged in their 30s; a situation which may reflect marital status (a known barrier to treatment) [13] and being self-employed, for whom treatment can interrupt their ability to make a living. In Japan, although economic aid is available for people who need treatment for HCV infection [3], further measures should still be considered to facilitate their visits to hepatologists. Additional work also needs to be done regarding potential prejudice for these infections in the workplace [14]. With regard to periodic visits to medical facilities for treatment of HCV infection, individuals who reported no visits accounted for the largest proportion, and this was explained by an absence of subjective symptoms and the absence of a doctor's recommendation to seek follow-up care. It is desirable for all primary care doctors in Japan, as elsewhere, to ensure that HCV carriers whom they see in their practice undergo appropriate follow-up by hepatology specialists [15].

Table 3.Characteristics of hepatitis C virus (HCV) carriers<br/>with no treatment history.

	%	(95%CI)**
Gender		
Male	26.9	(19.9-33.9)
Female	44.9	(37.0-52.7)
Age		
20-29	25	(0-55.0)
30-39	55.6	(42.2-69.0)
40-49	37.8	(27.5-48.1)
50-59	32.2	(23.5-40.8)
60-69	30	(17.8-42.2)
Occupation		
Company Employee	33.8	(26.9-40.7)
Self-employed	34.4	(21.5-47.3)
Part-time	40.9	(30.0-51.7)
HCV Infection Status Discovery		
At a regular health check-up (n=46)	37	(23.0-51.0)
At the time of health screening for pregnancy or pre-surgical screen- ing (n=34)	41.2	(24.7-57.7)
At visit to a medical facility be- cause of ill health (n=44)	38.6	(24.2-53.0)
At the time of blood donation (n=22)	13.6	(0-27.9)
At visit to a medical facility prompted by anxiety regarding blood transfusion or use of blood products in the past (n=9)	44.4	(11.9-76.9)
Other Reason (n=5)	46.2	(19.1-73.3)

\*n=56

\*\*95% Confidence Intervals

Although it was one of the first of its kind in Japan, the current study had certain limitations that must be taken into consideration when interpreting the results. Firstly, as it was a web-based survey, the participants we recruited had access to the internet and had volunteered to participate in such a survey – conditions which may in turn, impart a certain degree of selection bias. Secondly, given the fact that we investigated a sub-section of a sub-section of the community, our sample size was rather small. As a result, further investigations of a larger scale are now necessary to establish the national Japanese situation. Thirdly, our study utilized self-reported data on all responses, especially with regard to HCV status and could thus, not be verified by objective laboratory data. To address this issue in future research, HCV-RNA status will need to be clinically established.

## CONCLUSION

In conclusion, the current study suggests that a considerable proportion of Japanese HCV carriers have never received treatment for their infection. No official systems currently exist in Japan which will prompt HCV carriers to visit specialists in hepatology, even for those whose infections are confirmed by laboratory testing. This clearly needs to be addressed at a national level. Intervention is also necessary for members of the Japanese population who have already been diagnosed as HCV carriers but who are not receiving any treatment or regular clinical follow-up.

# **CONFLICT OF INTEREST**

The authors confirm that this article content has no conflict of interest.

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