# Prevalence of hepatitis C virus infection among health-care workers: A 10-year survey

ANDREA MARCONI[1-4], SAVERIO CANDIDO[1], RENATO TALAMINI[3], MASSIMO LIBRA[1], FERDINANDO NICOLETTI[1], DEMETRIOS A. SPANDIDOS[4], FRANCA STIVALA[1] and LIDIA PROIETTI[2]

Departments of [1]Biomedical Sciences, and [2]Internal Medicine and Systemic Diseases, University of Catania, Catania; [3]Epidemiology and Biostatistics Unit, National Cancer Institute, IRCCS, Aviano (PN), Italy; [3]Department of Virology, Medical School, University of Crete, Heraklion, Greece

Received March 19, 2010; Accepted April 30, 2010

DOI: 10.3892/mmr_00000297

**Abstract.** Hepatitis C virus (HCV) is one of the most common blood-borne pathogens transmitted from patients to health-care workers (HCWs). HCV infection status among HCWs and occupational blood exposure accidents were monitored to assess the risk of HCV infection among 403 HCWs from a single institution between 1999 and 2009. Additionally, HCV-related malignancies were evaluated in the HCV-positive HCWs. HCV infection was detected in 3% of the subjects at the first survey. The HCWs that initially tested negative for HCV remained negative during the 10 years of the survey. Of note, a statistically significant decrease was observed in the number of HCWs that experienced occupational blood exposure accidents, from 116 in 1999 to 72 in 2009 (p=0.0002). One HCV-infected HCW developed B-cell non-Hodgkin lymphoma (NHL) of the liver. The heavy chain gene combinations detected in the DNA from the NHL tissue were of the type usually found in HCV-associated lymphomas, supporting the role of HCV infection in the lymphomagenesis of this patient. The set of universal precautions recommended by the US Center for Disease Control and Prevention aided in the prevention of HCV transmission from patients to HCWs, as all 390 HCV-negative HCWs remained negative for the duration of the survey. Consequently, these recommendations also serve to prevent the development of HCV-associated malignancies such as hepatocellular carcinoma or B-cell NHL.

## Introduction

Health-care workers (HCWs) are at an increased risk of exposure to blood-borne pathogens. Hepatitis C virus (HCV) is one of the most common viruses transmitted from patients to HCWs. The frequency of HCV-positive blood donors ranges from 0.5-1.5% among industrialised nations in North America, Western Europe and Asia, and is believed to be higher among the general population (1,2). HCV infection contributes to chronic liver disease in many individuals worldwide.

Numerous studies have described the risk of HCV infection among HCWs. HCV may be transmitted by exposure to blood, semen and cerebral spinal fluid (3-5). Percutaneous HCV transmission may occur following needle-stick injures or cuts from other sharp instruments. Transmission may also occur after exposure of the eyes, nose, mouth or broken skin to HCV. The risk of infection varies with the type of exposure and other risk factors. Factors that increase the risk of HCV transmission from percutaneous exposure include a deep injury, visible blood on a surgical device, procedures involving placement of a needle directly into a blood vessel, and a high plasma viral load in the host. Transmission occurs in 3-10% of cases of percutaneous exposure to HCV (6-8).

Analysis of the risk factors for HCV infection among HCWs has generated conflicting results. In a previous study, 2% of dentists and 9% of oral surgeons were shown to be positive for anti-HCV antibodies. The probability of being positive for anti-HCV antibodies increased with an increase in the percentage of professional time spent practising oral surgery. However, dentists positive for anti-HCV antibodies reported 50% fewer needlesticks injures during the preceding 5 years than dentists negative for anti-HCV antibodies. By contrast, among hospital-based HCWs, positivity for anti-HCV antibodies was more common in HCWs that reported a history of frequent needlestick injuries (9,10).

In the last two decades, several studies have indicated that, in addition to contributing to the development of hepatocellular carcinoma (already largely demonstrated) (11) HCV infection may contribute to the development of non-Hodgkin lymphoma (12). In 1988, the US Center for Disease Control and Prevention developed a set of universal safety measures to prevent the transmission of blood-borne pathogens between patients and HCWs in a health care setting (13,14). Implementation of these precautions may decrease HCV transmission between patients and HCWs.

In the present study, the number of HCWs from a single institution reporting occupational blood exposure accidents over the 10 years of the survey (1999-2009) was compared

*Correspondence to:* Dr Massimo Libra, Department of Biomedical Sciences, University of Catania, Via Androne 83, 95124 Catania, Italy
E-mail: mlibra@unict.it

*Key words:* hepatitis C virus, health-care worker, non-Hodgkin lymphoma, surveillance

Table I. Hepatitis C virus (HCV) infection status of health-care workers according to professional categories.

| Professional categories | HCV-Positive | | HCV-Negative | | Total |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Nurse | 7 | 3 | 233 | 97 | 240 |
| Physician/Surgeon | 5 | 5 | 90 | 95 | 95 |
| Other | 1 | 1.5 | 67 | 98.5 | 68 |
| Total HCWs | 13 | 3 | 390 | 97 | 403 |

Table II. Number of subjects from each profession reporting accidental blood exposure while working during 1999 and 2009.

| Professional categories (n) | 1999 | | 2009 | | P-value[a] |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Nurse (240) | 58 | 24 | 34 | 14 | 0.0050 |
| Physician or surgeon (95) | 51 | 53 | 37 | 39 | 0.0400 |
| Other HCWs (68) | 7 | 10 | 1 | 1 | 0.0300 |
| Total HCWs (403) | 116 | 28 | 72 | 18 | 0.0002 |

[a]Determined using the $\chi^2$ test. HCWs, health-care workers.

to evaluate whether there was a change in the incidence of these accidents. In conjunction, the HCV infection status of the HCWs was analyzed in 1999 and 2009 to determine the number of HCWs infected with HCV during this period. Additionally, in the HCV-positive HCWs, occurrences of HCV-related malignancies were evaluated. The lifestyle risk factors of the HCV-positive HCWs were analyzed to address the possibility that infection may not have resulted from occupational exposure to the viral agent.

## Materials and methods

The subjects included 403 employees of an Italian public hospital. All were HCWs at high risk of exposure to blood-borne pathogens. The lifestyle risk factors for HCV infection were assessed by asking each subject whether they had lived with an HCV-positive partner, had received a blood transfusion, had a history of casual sexual intercourse, had any tattoos, or had a history of intravenous drug abuse. Subjects were also asked whether they had experienced accidental blood exposure while working between 1999 and 2009. The proportion of subjects reporting accidents in 1999 vs. 2009 was compared. The $\chi^2$ test was used to determine the presence of a statistically significant difference. Peripheral blood from all subjects was screened for anti-HCV antibodies by an enzyme-linked immunosorbent assay (Ortho Diagnostic Systems, Raritan, NJ, USA) as previously described (15). The HCWs were also examined for HCV-related malignancies.

*Analysis of B-cell clones*. To determine B-cell clonality in a non-Hodgkin lymphoma (NHL) sample from an HCV-positive HCW, complementary determining region-3 (CDR3) of the Ig heavy chain gene was amplified by PCR. The upstream primer was complementary to framework region-3 (FR3) of the VH, while the downstream primer was complementary to the JH. Ig heavy chain gene DNA was amplified by PCR with upstream primers complementary to framework region-1 (FR1) of each VH gene segment family and with a downstream primer complementary to CDR3 (16). PCR products were purified by gel electrophoresis, then sequenced. The most similar VH and DH germline gene segments were identified by sequence comparison to the International Immunogenetics Database with DNAplot software (http://imgt.cines.fr).

*Immunophenotyping*. Paraffin sections were used for the immunophenotyping and lineage assignment of the NHL case. The sources and specificities of the antibodies used in this study have been reported in detail previously (17).

## Results

The HCWs included 240 (59%) nurses, 95 (24%) physicians and surgeons and 68 (17%) other employees (laboratory technicians, midwives and rehabilitation therapists). HCV infection was detected in 13 (3%) HCWs at the first analysis in 1999. The frequency of HCV-infection at the first observation according to professional categories was 5% of physicians and surgeons and 3% of nurses (Table I). The remaining 390 HCWs remained HCV-negative at the final analysis in 2009. None of the HCV-positive HCWs experienced accidental blood exposure while working in 1999 or 2009. However, some HCV-positive HCWs did report percutaneous blood exposure while working prior to 1999. HCV-positive HCWs did not report any of the lifestyle risk factors for HCV infec-

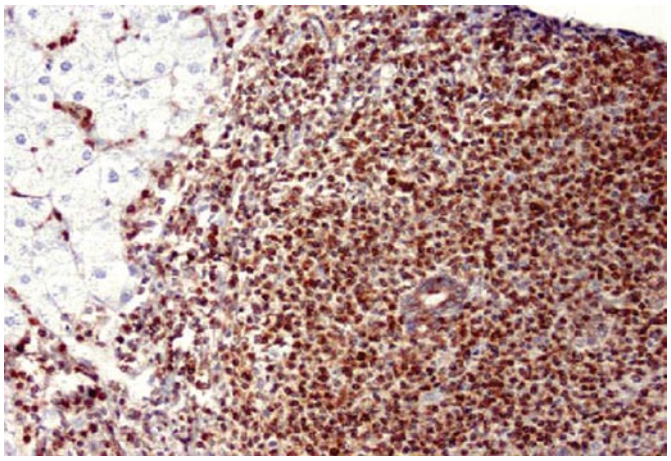

Figure 1. Bcl-2 immunostaining of mucosa-associated lymphoma tissue (MALT) of the liver.

tion. Occupational blood exposure accidents prior to 1999 were reported by 30% of HCV-negative HCWs. Approximately 80% of the occupational blood exposure accidents documented were percutaneous injures, while contact between blood and skin or between blood and mucous membranes was reported in approximately 13 and 6% of occupational blood exposure accidents, respectively (data not shown). A statistically significant decrease in the number of occupational blood exposure accidents occurring in 1999 compared to 2009 was documented among the HCWs (116 vs. 72; p=0.0002) (Table II).

Of note, one 62-year-old HCV-positive male nurse was diagnosed in 2008 with a mucosa-associated lymphoma tissue (MALT) of the liver. To elucidate whether HCV infection is associated with the development of this B-cell lymphoproliferation, a molecular analysis of a B-cell clone was performed. Neoplastic B-cell expansion expressed VH4-69-DH2-15-JH2 Ig heavy chain genes according to the IMGT database.

*Immunophenotyping*. The tumours analyzed were $CD20^+$, cyclin $D1^-$, $CD23^-$, $CD5^-$, $Bcl\text{-}6^-$, $CD43^-$ and $CD10^-$, supporting the diagnosis of a MALT lymphoma. In particular, the null expression of CD10 and Bcl-6 excluded a follicular origin for the tumour; the overexpression of Bcl-2 suggested that the t(14;18) translocation, usually linked to HCV-associated lymphomas, may sustain the survival of B-cells, thus preventing apoptosis (Fig. 1).

## Discussion

HCV is one of many blood-borne pathogens that HCWs may be exposed to. Infection by this virus leads to chronic or fatal illnesses, which are expensive and difficult to treat. The aim of the present study was to investigate the prevalence of HCV infection among HCWs along with work-related biological risk accidents during a 10-year survey. As shown in Table I, although the low number of HCV-infected individuals prevents the assessment of statistical significance, the prevalence of infection appears to be among nurses and physicians, including surgeons, in comparison to the other HCW categories. However, it could be argued that all of the HCW categories analyzed carry a similar risk of virus infection. No new infections were detected during the 10 years of observation. Notably, in 1999 and 2009 we observed a significant reduction in the occurrence of biological risk accidents across all professional categories. Lifestyle risk factors for HCV infection were not accountable for virus transmission among HCV-positive HCWs, as the HCWs did not report any risk besides the professional exposure. Our findings are in agreement with previous results indicating that the education of HCWs on the prevention of needle-stick accidents along with effective communication and convenient placement of containers decreases needle-stick injuries (18). Although exposure prevention remains the best strategy for protecting HCWs from occupationally acquired infection, exposure is nevertheless likely to occur. To minimize the risk of blood-borne pathogen transmission from patients to HCWs (and vice versa), all HCWs should adhere to standard precautions, including the appropriate use of hand washing, protective barriers (e.g., gloves), and care in the use and disposal of needles and other sharp instruments. Employers should implement a system including written protocols for prompt reporting, evaluation, counselling, treatment and follow-up of occupational exposure that may place a worker at risk of blood-borne pathogen infections (8).

Chronic HCV infection has been demonstrated to be responsible for hepatic (12) and extra-hepatic disorders (11,19); therefore, in the present study, we screened HCV-positive HCWs for the presence of such diseases. One nurse developed a MALT of the liver after 25 years of HCV chronic infection. Interestingly, the heavy chain gene combinations detected in the DNA from the MALT tissue were those usually found in HCV-associated lymphomas, suggesting that the HCV infection played a role in the lymphomagenesis (19). Accumulating evidence supports a model in which chronic stimulation of B-cells by antigens associated with HCV infection causes non-malignant B-cell expansion that may evolve into B-cell NHL. Immunohistochemistry analysis revealed that the null expression of CD10 and Bcl-6 excludes a follicular origin of this tumour. This is in agreement with previous studies, as a follicular lymphoma histotype is uncommon among HCV-infected patients (15). Moreover, the overexpression of Bcl-2 detected in this MALT tissue suggests that the t(14;18) translocation, usually linked to HCV-associated lymphomas (20), may sustain the survival of B-cells, thus preventing apoptosis.

Finally, our data indicate that guidelines outlining standard precautions to reduce the risk of blood-borne pathogen transmission have a strong efficacy among HCWs.

## Acknowledgements

This work was supported in part by the Lega Italiana per la Lotta ontro i Tumori.

## References

1. Janot C, Courouce AM and Maniez M: Antibodies to hepatitis C virus in French blood donors. Lancet 30: 796-797, 1989.
2. Conry-Cantilena C, van Raden M, Gibble J, *et al*: Routes of infection, viremia, and liver disease in blood donors found to have hepatitis C virus infection. N Engl J Med 334: 1691-1696, 1996.

3. Klein RS, Freeman K, Taylor PE and Stevens CE: Occupational risk for hepatitis C virus infection among New York City dentists. Lancet 338: 1539-1542, 1991.
4. Kiyosawa K, Sodeyama T, Tanaka E, *et al*: Hepatitis C in hospital employees with needlestick injuries. Ann Intern Med 115: 367-369, 1991.
5. Mitsui T, Iwano K, Masuko K, *et al*: Hepatitis C virus infection in medical personnel after needlestick accident. Hepatology 16: 1109-1114, 1992.
6. Riddell LA and Sherrard J: Blood-borne virus infection: the occupational risks. Int J STD AIDS 11: 632-639, 2000.
7. Torbati SS and Guss DA: Emergency department management of occupational exposures to HIV-infected fluids. J Emerg Med 17: 261-264, 1999.
8. Beltrami EM, Williams IT, Shapiro CN and Chamberland ME: Risk and management of blood-borne infections in health care workers. Clin Microbiol Rev 13: 385-407, 2000.
9. Polish LB, Tong MJ, Co RL, Coleman PJ and Alter MJ: Risk factors for hepatitis C virus infection among health care personnel in a community hospital. Am J Infect Control 21: 196-200, 1993.
10. Panlilio AL, Shapiro CN, Schable CA, *et al*: Serosurvey of human immunodeficiency virus, hepatitis B virus, and hepatitis C virus infection among hospital-based surgeons. Serosurvey Study Group. J Am Coll Surg 180: 16-24, 1995.
11. Bartosch B, Thimme R, Blum HE and Zoulim F: Hepatitis C virus-induced hepatocarcinogenesis. J Hepatol 51: 810-820, 2009.
12. Negri E, Little D, Boiocchi M, La Vecchia C and Franceschi S: B-cell non-Hodgkin's lymphoma and hepatitis C virus infection: a systematic review. Int J Cancer 111: 1-8, 2004.
13. Center for Diseases Control and Prevention (CDC): Recommendations 5 for prevention and control of hepatitis virus (HCV) infection and HCV-related chronic disease. MMWR Recomm Rep 47: 1-39, 1998.
14. Center for Diseases Control and Prevention (CDC): Notice to readers recommendations for follow-up of health-care workers after occupational exposure to hepatitis C virus. MMWR Recomm Rep. 46: 603-606, 1997.
15. Talamini R, Montella M, Crovatto M, *et al*: Non-Hodgkin's lymphoma and hepatitis C virus: a case-control study from northern and southern Italy. Int J Cancer 110: 380-385, 2004.
16. Libra M, Gloghini A, De Re V, *et al*: Aggressive forms of non-Hodgkin's lymphoma in two patients bearing coinfection of Epstein-Barr and hepatitis C viruses. Int J Oncol 26: 945-950, 2005.
17. Carbone A, Cilia AM, Gloghini A, *et al*: Establishment of HHV-8-positive and HHV-8-negative lymphoma cell lines from primary lymphomatous effusions. Int J Cancer 73: 562-569, 1997.
18. Haiduven DJ, DeMaio TM and Stevens DA: A five-year study of needlestick injuries: significant reduction associated with communication, education, and convenient placement of sharps containers. Infect Control Hosp Epidemiol 13: 265-271, 1992.
19. Libra M, Gasparotto D, Gloghini A, Navolanic PM, De Re V and Carbone A: Hepatitis C virus (HCV) infection and lymphoproliferative disorders. Front Biosci 10: 2460-2471, 2005.
20. Libra M, Gloghini A, Malaponte G, *et al*: Association of t(14;18) translocation with HCV infection in gastrointestinal MALT lymphomas. J Hepatol 49: 170-174, 2008.