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SHORT COMMUNICATION

Prevalence and characteristics of hepatitis C virus infection detected by extended screening of working-age adults in Madrid (Spain)

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1 | INTRODUCTION

Hepatitis C virus (HCV) infection is a leading cause of chronic hepatitis and its long-term complications of cirrhosis, liver failure and hepatocellular carcinoma.[1] The World Health Organization (WHO) estimates that 1% of the world population is infected with HCV.[2] In the European Union (EU), the estimated prevalence of HCV infection is 1.1%.[3] The availability of direct-acting anti-HCV antivirals (DAA) that achieve virological cure in more than 95% of treated individuals provides the opportunity to change the natural history of HCV infection and reduce its transmission.[4] However, only 20% of HCV-infected individuals are aware of their HCV status, and 7.4% of those are treated with DAA.[2] In 2016, the WHO and the EU endorsed a global strategy for the elimination of viral hepatitis by 2030[2,3]; policies for expanded testing are essential pillars of this strategy.

Screening for HCV infection has been traditionally restricted to certain groups, including adults born between 1945 and 1965 ("birth-cohort" group), and individuals with behaviours, exposures or conditions associated with increased risk for HCV infection. These recommendations have recently been updated to include all persons 18 years or older and pregnant women during each pregnancy.[5] However, screening for HCV infection in Spain is limited to blood, cells or tissue donors, and individuals at risk for this infection.[6] Until universal screening for HCV infection is instituted, prevalence studies in different populations are useful for the development of strategies for the identification and referral to treatment of HCV-infected individuals.

Our institution provides medical care to individuals who suffer work-related injuries or diseases. We routinely screen for HCV infection in all patients requiring surgical treatment and individuals exposed to biological fluids. This study is aimed to analyse the prevalence and characteristics of HCV infection among our population of working-age adults.

2 | MATERIALS AND METHODS

2.1 | Study design

Observational, retrospective cohort study at a single institution during a 6-year period (2013–2018).

2.2 | Study subjects

Individuals undergoing a surgical treatment or evaluated after occupational exposures to biological fluids were included. Data collected were study year, age, sex, past history of HCV infection, HCV antibody status, HCV RNA level and serum transaminase levels. The study was conducted in accordance with the standards

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TABLE 1 Characteristics of HCV infection in 228 working-age adults in Madrid (Spain)

	All		Known[a]		Unknown		Active[b]		
	Number	%	Number	%	Number	%	Number	%	p^c
	228	**100.0**	**134**	**58.8**	**94**	**41.2**	**41**	**44.1**	**.217**
Age (years)									
19–29	3	1.3	1	0.7	2	2.1	2	4.9	.504
30–39	20	8.8	14	10.4	6	6.4	3	7.3	
40–49	86	37.7	50	37.3	36	38.3	13	31.7	
50–59	109	47.8	62	46.3	47	50.0	21	51.2	
60–69	8	3.5	6	4.5	2	2.1	1	2.4	
70–79	2	0.9	1	0.7	1	1.1	1	2.4	
Birth cohort									
Yes	117	51.3	67	50.0	50	53.2	23	56.1	.857
No	111	48.7	67	50.0	44	46.8	18	43.9	
Sex									
Male	191	83.8	112	83.6	79	84.0	36	87.8	.631
Female	37	16.2	22	16.4	15	16.0	5	12.2	
Serum transaminases[d]									
Normal	161	72.2	99	75.0	62	68.1	16	42.1	<.001
Elevated	62	27.8	33	25.0	29	31.9	22	57.9	

[a] Known and unknown infections were defined, respectively, by present or absent evidence of HCV infection in the patient´s medical record; active HCV infection was defined by the presence in serum of detectable HCV RNA.

[b] HCV RNA was measured only in 93 of the 94 subjects with unknown HCV infection.

[c] Fisher's exact test.

[d] Serum transaminases were measured in 223 subjects, including 132 with known infection, 91 with unknown infection, and 38 with active infection.

of the hospital research committee and in compliance with the Declaration of Helsinki of 1974, revised in 2013. All participants gave written informed consent.

2.3 | Laboratory studies

Hepatitis C virus antibodies were measured by a chemiluminescence immunoassay (ARCHITECT anti-HCV, Abbott Laboratories). HCV antibody-positive individuals with previously known HCV infection were not further studied. Serum samples from HCV antibody-positive subjects unaware of their HCV status were further analysed for the presence of HCV RNA by a reverse transcriptase-polymerase chain reaction method (Abbott m2000, Abbott Molecular); results were expressed as $\log_{10}$ IU/ml. Serum transaminases were measured using a Cobas® c501 autoanalyzer (Roche Diagnostics); results were expressed in U/L.

2.4 | Definitions

Hepatitis C virus infection was defined by the presence of HCV antibodies. Known and unknown HCV infections were defined, respectively, by present or absent evidence of HCV infection in the patient´s medical record. Active HCV infection was defined by the presence in serum of detectable HCV RNA.

2.5 | Statistical analysis

Descriptive analysis of the demographic characteristics of the study participants was performed. Categorical variables are expressed as frequency rates and percentages, and continuous variables are expressed as mean and standard deviation (SD). Proportions of categorical variables were compared using the chi-square test, and Fisher's exact test was used to assess differences among sex, age group and serum aminotransferase levels. A binary logistic regression model was used to study the relationship between aminotransferase levels and active infection using odds ratio (OR) with 95% confidence interval (CI). All statistical analyses were performed with SPSS, version 21.0 (IBM Corp) for Windows. A two-sided p value < .05 was considered statistically significant.

2.6 | Link to medical care

Individuals previously unaware of their HCV status were referred to their primary care physician for follow-up and treatment.

3 | RESULTS

During the study period, 16,734 consecutive patients were analysed (Appendix 1). Two hundred and twenty-eight (1.4%) subjects were HCV antibody-positive, indicating past or current infection. There were 191 (83.8%) males and 37 (16.2%) females, with a mean (SD) age of 49.2 (7.5) years. One-hundred and thirty-four subjects (58.8%) had previously known HCV infection, and 94 (41.2%) participants were unaware of their HCV status. HCV RNA was measured in 93 subjects with unknown infections; of those, 41 (44.1%) had detectable HCV RNA [mean (SD) $\log_{10}$ HCV RNA UI/ml: 5.6 (1.1)]. Overall, serum transaminases were elevated in 62 (27.8%) subjects, including 22 (57.9%) of the subjects with active HCV infection (OR: 4.829; 95% CI: 2.3–10.03; $p < .001$). Data are summarized in Table 1.

4 | DISCUSSION

The prevalence of HCV infection in our study was 1.4%, similar to the prevalence in the general population described in other reports.[2,7] The reported prevalence of HCV infection among the general population in Spain is 0.69% to 1.2%.[8,9] Notably, 41.2% of HCV antibody-positive subjects in our study were not aware of their HCV infection, and 44.1% of those were viraemic. Also observed in other studies,[7,9] these findings establish the potential for transmission of HCV from a significant fraction of individuals who are unaware of their HCV status and reinforce the recent recommendation for universal screening for HCV infection.[5]

Almost half of HCV antibody-positive patients in our study did not belong to the birth-cohort group; in contrast, the prevalence of active HCV infection was higher in the birth-cohort group as compared to the rest of study subjects. Although these differences were not statistically significant, our results indicate that testing for HCV infection limited to individuals belonging to the birth-cohort group would have missed a significant proportion of HCV-infected subjects, including some with viraemia. These findings underscore the importance of extending HCV screening beyond traditional risk group categories for this infection.

We found that serum transaminases were elevated in only a quarter of HCV antibody-positive individuals but in more than half of those with HCV viraemia. These results indicate that elevated serum transaminase levels are not a useful marker for HCV infection but increase the likelihood of viraemia in HCV-infected subjects.

The recommended diagnostic sequence for HCV infection includes detection of antibodies followed by reflex testing of positive samples for HCV RNA.[10] In our study, HCV RNA was not detected in 56% of HCV-infected individuals who were not aware of their infection status. The absence of viraemia in these untreated HCV antibody-positive subjects could indicate either a resolved past infection or a false-positive antibody test result.[3] In this situation, the decision for additional follow-up testing should be individualized.

Our study has several limitations. First, the results might not be representative of the general population. We studied subjects who underwent surgical interventions following work-related injuries or with occupational exposure to biological fluids; therefore, the 1.4% prevalence we found might be an overestimate of the true prevalence of HCV infection in the general population. Second, risk factors for HCV infection of the subjects included in the study (other than year of birth) were not collected. Third, most of the individuals we studied were male and the majority were 40–60 years old; therefore, women and younger and older individuals were underrepresented. Fourth, it is possible that the proportion of unknown HCV infection was overestimated because the HCV status of the patients might not have been accurately collected in their medical records; however, the high HCV RNA levels in the subjects with viraemia in our study suggest that their infections were untreated and most likely, truly unknown. Finally, we did not collect follow-up information on HCV-infected patients after their referral to primary care physicians.

Based on our results, we recommend that clinicians use any opportunity to screen their patients for HCV infection. By adopting this policy, HCV-infected individuals who are unaware of their HCV status could be identified and offered curative therapy with DAA.[3] In addition, identification of subjects with unknown HCV infections is the necessary first step to control the transmission of HCV.

In conclusion, extended screening of working-age adults for HCV infection detected a significant proportion of HCV-infected individuals with viraemia and normal serum transaminase levels, who were unaware of their infection status. The results of this study support the importance of universal screening for HCV infection.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this work.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon request.

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APPENDIX 1

Results of screening for HCV infection during the study period (2013–2018)

			HCV infections[a]							
	Subjects studied		All		Known		Unknown		Active[b]	
	Number	%	Number	%	Number	%	Number	%	Number	%
	16,734	**100.00**	**228**	**1.362**	**134**	**0.801**	**94**	**0.562**	**41**	**0.002**
Age (years)										
19–29	1,873	11.19	3	0.16	1	0.05	2	0.11	2	0.11
30–39	4,195	25.07	20	0.48	14	0.33	6	0.14	3	0.07
40–49	5,434	32.47	86	1.58	50	0.92	36	0.66	13	0.24
50–59	4,266	25.49	109	2.56	62	1.45	47	1.10	21	0.49
60–69	942	5.63	8	0.85	6	0.64	2	0.21	1	0.11
70–79	24	0.14	2	8.33	1	4.17	1	4.17	1	4.17
Birth cohort										
Yes	5,258	31.42	117	2.23	67	1.27	50	0.95	23	0.44
No	11,476	68.58	111	0.97	67	0.58	44	0.38	18	0.16
Sex										
Male	11,830	70.69	191	1.61	112	0.95	79	0.67	36	0.30
Female	4904	29.31	37	0.75	22	0.45	15	0.31	5	0.10

[a]Known and unknown infections were defined, respectively, by present or absent evidence of HCV infection in the patient´s medical record; active HCV infection was defined by the presence in serum of detectable HCV RNA.[b] HCV RNA was measured only in 93 of the 94 subjects with unknown HCV infection.