CrossMark

SHORT REPORT High prevalence of hepatitis C (HCV) in the emergency department (ED) of a London hospital: should we be screening for HCV in ED attendees?

C. ORKIN¹*, E. LEACH², S. FLANAGAN¹, E. WALLIS¹, M. RUF³, G. R. FOSTER⁴ AND C. Y. W. TONG⁵

¹Department of Infection and Immunology, The Royal London Hospital, Barts Health NHS Trust, London, UK

² Department of Biochemistry, The Royal London Hospital, Barts Health NHS Trust, London, UK

³ Department of Medical Affairs, Gilead Sciences Ltd, Uxbridge, Middlesex, UK

⁴Blizard Institute of Cell and Molecular Science, Queen Mary University London, London, UK

⁵ Department of Virology, The Royal London Hospital, Barts Health NHS Trust, London, UK

Received 2 December 2014; Final revision 8 January 2015; Accepted 21 January 2015; first published online 12 February 2015

SUMMARY

An unlinked anonymous study was conducted to estimate the prevalence of hepatitis C virus (HCV) infection in emergency department (ED) attendees at a London Hospital. Nine hundred and ninety-seven samples collected over a 12-day period were tested for HCV antibody (Ab) and reactive samples were further tested for HCV RNA. The HCV seroprevalence was 2.6% (26/997) with 1.2% (12/997) HCV RNA positive. A peak HCV RNA-positive prevalence of 4.8% (3/63) was found in males aged 35–44 years, this was compared to 0% (0/136) in males aged <35 years (P = 0.0614) and 1.4% (4/278) in males aged ≥ 45 years (P = 0.2415). Assuming the cost for HCV Ab is £6 and HCV RNA is £40 per test, screening ED attendees aged 25–54 years would cost £360 per viraemic infection and identify 82% of those who were HCV RNA positive, yielding the most favourable cost/benefit ratio. HCV screening of ED attendees aged 25–54 years in this population could be an effective way of identifying patients and limit onward transmission.

Key words: Emergency department, HCV RNA-positive prevalence, hepatitis C, screening, seroprevalence.

Hepatitis C virus (HCV) is a major public health problem with about 130–170 million people infected worldwide [1]. In England the prevalence of HCV is estimated to be 0.4% with 160 000 individuals chronically infected [2], a quarter of whom live in London [3]. The health burden of HCV is apparent with HCV-related end-stage liver disease hospitalizations, hepatocellular carcinoma, liver transplants and deaths rising year on year [2]. New expensive direct-acting antiviral therapies, offering cure rates close to 100% [4], are tolerable with shorter treatment duration [5]. The ideal of eradication of the HCV epidemic must remain a goal.

In the UK, half of those infected with HCV are undiagnosed [3]. In the context of HIV, universal screening is recommended in medical settings where the local prevalence is >2/1000 population [6]. In contrast to the US Centre for Disease Control and Prevention (CDC) recommendations for birth cohort population screening in healthcare settings, there are no systematic HCV screening recommendations in the UK in general healthcare settings. The UK National Institute for Health and Care Excellence

^{*} Author for correspondence: Dr C. Orkin, Grahame Hayton Unit, The Royal London Hospital, Whitechapel, London, El 1BB, UK. (Email: Chloe.orkin@bartshealth.nhs.uk)

Age group, yr	Total cohort (<i>n</i>)	Male patients (n)	Reactive HCV Ab (<i>n</i>)	HCV Ab prevalence (%)	HCV RNA positive (n)	HCV RNA prevalence (%)	Male positive HCV RNA (<i>n</i>)	Male specific RNA prevalence (%)
15–24	92	42	0	0.00%	0	0.00%	0	0.00%
25-34	177	94	2	1.10%	2	1.13%	0	0.00%
35-44	128	63	7	5.50%	3	2.34%	3	4·76%
45-54	136	81	6	4.40%	4	2.94%	2	2.47%
55-64	108	51	2	1.90%	0	0.00%	0	0.00%
65–74	118	60	3	2.50%	1	0.85%	1	1.67%
>75	158	86	3	1.90%	1	0.63%	1	1.16%
Unknown age	80	64	3	3.80%	1	1.25%	1	1.56%
Total	997	541	26	2.61%	12	1.20%	8	1.48%

 Table 1. Age- and gender-specific HCV Ab and HCV RNA prevalence

(NICE) recommendations are essentially risk-based HCV testing as well as the development of services for areas where the population includes a higher than average number of people at increased risk [7]. Furthermore, data from Public Health England HCV sentinel surveillance indicate very little testing is currently occurring in the emergency department (ED) [8]. In 2013 there were 18.3 million attendances at EDs in England with 13% having bloods taken [9], making it an obvious and accessible place to offer screening. In Europe, a Swiss HCV seroprevalence study of 5036 ED patients found a HCV antibody (Ab) positive rate of 2.7% [10]. A German study found seroprevalence of 2.5% with 1.6% RNA positive [11]. We aimed to establish the prevalence of active HCV infection in ED attendees using an anonymous seroprevalence approach in a busy urban London ED.

Residual biochemistry samples from London ED attendees aged >18 years were collected during a 12-day period in August 2014. Anonymization of samples and HCV testing were double-blinded. For each sample data on age, gender and ethnicity were collected and the sample was tested for HCV Ab using an automated EIA (Architect, Abbott, USA). Reactive samples were further tested for HCV RNA (COBAS Amplicor, Roche, USA). Data were statistically analysed using two-sided χ^2 test or Fisher's exact test as appropriate via OpenEpi v. 3.03 (www.openepi.com).

Nine hundred and ninety seven samples were collected during the study period. Overall, 26/997 (2.65%) were positive for HCV Ab and 12/997 (1.2%) were HCV RNA positive (see in Table 1). Excluding 80 patients with unknown age, there was no difference in median age between the total cohort (median age 47 years), and those who were HCV Ab positive (median age 47 years) or HCV RNA positive (median age 48 years). Fifty-four per cent (n = 541/997) of the cohort were male, 61.5% (n = 16/26) of the HCV Ab-positive group were males and 66.7% (8/12) of viraemic patients were male (P = 0.4). However, there was a substantial variation in age-/gender-specific RNA positivity peaking at 4.8% (3/63) in males aged 35-44 years, compared to 0% (0/136) in males aged <35 years (P = 0.0614) and 1.4% (4/278) in males aged ≥ 45 years (P = 0.2415).

Although 30% of those attending the ED were Asian (300/997) and 31% (311/997) white British, 58% (7/12) of HCV RNA-positive samples came from white British attendees. The prevalence of RNA-positive samples were higher in white British attendees (7/311, 2·3%) compared to only 0·3% (1/306) in Asian attendees, although this difference was not statistically significant (P = 0.0766).

To our knowledge this is the first study to provide HCV prevalence data for a UK population of ED attendees. We found the seroprevalence for HCV Ab to be 2.65%, sixfold higher than the stated national prevalence of 0.4% [2]. Furthermore, almost half (46%) of those found to be HCVAb positive were also HCVRNA positive and were therefore infectious to others. We found the gender-/age-specific HCV RNA-positive prevalence was at its highest (4.8%) in males aged 35-44 years. The age-/sex-specific HCV profile, although significantly higher, broadly reflects national patterns [8]. Assuming the cost for HCV Ab is £6 and HCV RNA is £40 per test (based on our local laboratory costing), screening ED attendees aged 25-54 years having bloods taken in this ED could identify 82% of those RNA positive at a cost of £360 per viraemic infection. This would be likely to yield the most favourable cost-benefit ratio in this ED population.

These results are in keeping with other European studies of HCV Ab prevalence in the ED in

Switzerland and Germany where the HCV Ab prevalence was 2.7% [10] and 2.5% [11], respectively. The German study of 28 809 ED patients found a HCV RNA prevalence of 1.6% and one fifth of the RNA-positive patients contacted were not previously aware of their diagnosis [11]. Although HCV prevalence is generally high in Asian ethnic groups [2], and 30% of ED attendees in this study were Asian, we found the greatest HCV Ab and HCV RNA prevalence to be in those of white ethnicity. Those described as white British made up 4.2% of positive HCV Ab and 2.3% of viraemic individuals, this is in stark contrast with the respective rates of 0.7% and 0.3% in Asian ED attendees. These findings, together with the epidemiological age profile of attendees may reflect ED usage patterns by urban white high-risk populations.

Given that 50% of our HCV population in the UK are undiagnosed [2] and better treatments exist [4, 5], these findings suggest a case for considering routine HCV screening in the ED in urban areas. Currently, HCV testing is not part of the routine testing algorithm for ED patients, unless specifically requested. Although NICE advocated increase HCV screening in areas with a high proportion of people at risk of hepatitis [7], there are no specific guidelines in place for routine opt-out screening.

ED HCV prevalence data are necessary but not sufficient to ensure HCV screening in the ED is justified. Other elements include patient and staff acceptance rates, rates of new diagnosis and linkage to care rates. Results from a US study examining the implementation of CDC recommended opt-out HCV testing guidance found high screen positivity, high patient acceptability and linkage to care rates of 55% [12].

Likely due to the relatively small sample size, the differences identified between age and ethnic groups did not reach statistical significance. In addition, this study does not offer data on the number of diagnosed HCV-infected ED attendees not already linked to care and the proportion of those identified as infected who attend for therapy will be critical in evaluating the value of this approach. Furthermore, the use of residual biochemistry samples introduces some selection bias and may under- or over-estimate HCV prevalence within this cohort. Moreover, the cost-benefit ratio would be affected by whether or not the viraemic patients were aware of their HCV status with the costbenefit ratio being slightly higher than the ratio stated depending on whether the viraemic patients need further confirmatory testing. Further research is therefore recommended to provide more data and to confirm our findings. As the findings in our population may not be applicable to EDs in other geographical locations, local data for EDs serving different patient populations need to be established for local HCV screening recommendations.

Our study demonstrated an unexpectedly high prevalence of active HCV infections in urban ED attendees in the UK especially in the 25–54 years age group. The study also found that in our population, white British subjects were most likely to have active HCV infection. Further research exploring feasibility and acceptability of introducing targeted opt-out screening and linkage to care is needed.

Ethical approval for this study was given by the Joint Research Management Office at Barts Health NHS on 7 August 2014 (REC reference number 14/EM/1118).

ACKNOWLEDGEMENTS

This work was supported by Gilead Sciences (grant no.: ReDA 009911). This paper has been submitted as an abstract to the European Association for the Study of the Liver conference on 9–13 April 2015.

DECLARATION OF INTEREST

G.R.F. has received funds from companies that sell drugs for the treatment of viral hepatitis including: BMS, BI, Gilead, Janssen, Novartis, Springbank, Achillion, GSK, AbbVie. C.O. has received funds from companies that sell drugs for the treatment of HIV including: Gilead, GSK, Boehringer-Ingleheim, BMS, Viiv, Jannsen, Johnson & Johnson, MSD, Abbott and AbbVie. S.F. has received course sponsorship from Merck. M.R. is employed by Gilead Science. Y.W.T., E.L. and E.W. have no conflict of interest.

REFERENCES

- 1. Hajarizadeh B, Grebley J, Dore GJ. Epidemiology and natural history of HCV infection. *Nature Reviews Gastroenterology and Hepatology* 2013; 10: 553–562.
- Public Health England. Hepatitis C in the UK: 2013 report. (http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317139502302). Accessed 24 November 2014.
- 3. Hepatitis C Trust. The uncomfortable truth. Hepatitis C in England: the state of the nation. 2013 (http://www.hepctrust.org.uk/Resources/HepC%20New/The%20Trust/The%20Uncomfortable%20Truth.pdf). Accessed 24 November 2014.

- 4. Lawitz E, et al. Sofosbuvir and ledipasvir fixed-dose combination with and without ribavirin in treatmentnaive and previously treated patients with genotype 1 hepatitis C virus infection (LONESTAR): an openlabel, randomised, phase 2 trial. *Lancet* 2014; **383**: 515–523.
- Dore GJ. The changing therapeutic landscape for hepatitis C. *Medical Journal of Australia* 2012; 196: 629–632.
- British HIV Association. UK national guidelines for HIV Testing. 2008 (http://www.bhiva.org/documents/ Guidelines/Testing/GlinesHIVTest08.pdf). Accessed 10 November 2014.
- National Institute of Clinical Excellence. Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection. 2014 (http://www.nice.org. uk/guidance/ph43/resources/hepatitis-b-and-c-ways-topromote-and-offer-testing-draft-guidance2). Accessed 11 November 2014.
- Public Health England. Annual report from the sentinel surveillance study of blood borne virus testing in England: data for January to December 2013. (https://

www.gov.uk/government/uploads/system/uploads/attachment_data/file/345716/hpr2914_senthep.pdf). Accessed 24 November 2014.

- 9. Hospital Episode Statistics. Accident and emergency attendances in England. Health and Social Care Information Centre. 2014 (http://www.hscic.gov.uk/ catalogue/PUB13464/acci-emer-atte-eng-2012-2013-rep. pdf) Accessed 24 November 2014.
- Russmann S, et al. Prevalence and associated factors of viral hepatitis and transferrin elevations in 5036 patients admitted to the emergency room of a Swiss university hospital: cross-sectional study, BMC Gastroenterology 2007; 7: 5.
- 11. Vermehren J, et al. High prevalence of anti-HCV antibodies in two metropolitan emergency departments in Germany: a prospective screening analysis of 28,809 patients. PLoS ONE 2012; 7: e41206.
- Galbraith JW, et al. Unrecognized chronic hepatitis C virus infection among baby boomers in the emergency department. *Hepatology*. Published online: 1 September 2014. doi:10.1002/hep.27410.