Improving surveillance for acute hepatitis C

Rachel M Deacon, Handan Wand, Sacha Stelzer-Braid, Carla Treloar, Lisa Maher

Abstract

Understanding patterns of newly acquired hepatitis C virus (HCV) infection is fundamental to assessing the impact of prevention and treatment interventions. However, identifying newly acquired cases is difficult, usually requiring documented testing before and after exposure. As the proportion of cases identified as newly acquired by current New South Wales surveillance methodologies is significantly lower than that identified nationally, the impact on the identification of newly acquired cases of systematic reporting of past negative HCV test results from notifying laboratories was assessed. HCV notifications data for 2007 from two New South Wales laboratories were analysed. Cases with a negative HCV antibody test within the past 24 months were classified as newly acquired. These were linked to the NSW Department of Health (NSW Health)-identified cases to assess the effectiveness of accessing laboratory data. The laboratories accounted for approximately half of all new HCV notifications in 2007. Of the 2,206 newly diagnosed cases, 21 (1.0%) were newly acquired, 18 of which had not been identified under the current surveillance system, increasing the total number of newly acquired cases to 83 from 65. This increased the yield by 28% and increased the proportion of newly acquired cases from 65/4,192 (1.6%) to 83/4,196 (2.0%). Laboratory-identified cases were significantly more likely than NSW Health-identified cases to be aged 30 years or over. Combined with current reporting mechanisms, laboratory data on previous HCV test results have the potential to increase the number of newly acquired cases identified through the New South Wales surveillance system and to enhance the identification of cases among those aged 30 years or more. *Commun Dis Intell* 2011;35(1):16–20.

Keywords: hepatitis C virus, epidemiology, surveillance

Introduction

Hepatitis C virus (HCV) infection affects approximately 3% of the world's population and is globally a major cause of morbidity and mortality among people who inject drugs.[1–2] In Australia, HCV infection is notifiable in all states and territories. A total of 11,319 notifications of HCV infection were made in 2008, making HCV the fourth most common notifiable disease.[3]

Improved identification of newly acquired cases of HCV infection, demographic characteristics and risk factors have the potential to inform prevention and treatment activities.[4–6] Further, recent data suggest treatment of acute HCV infection results in higher rates of virological clearance than treatment of chronic infections.[7] The National Notifiable Diseases Surveillance System (NNDSS) definition for newly acquired HCV,[8] used by all Australian states and territories, is summarised in the Box. Identifying a positive HCV antibody or RNA test result from a patient as newly acquired requires a documented negative HCV antibody test or clinical evidence of acute hepatitis where other causes have been excluded, within the past 24 months. As acute hepatitis is present only in a minority of cases,[9] newly acquired cases are difficult to identify. However, between 2004 and 2006 the Victorian HCV surveillance system approximately doubled the rate of identification of newly acquired HCV cases (from 3%–5% in 2004–2005, to 6%–8% in 2006–2009)[10–11] by implementing laboratory follow-up for all HCV cases aged less than 30 years.

Of approximately 4,000 cases of newly diagnosed HCV reported in New South Wales each year, current surveillance methodologies identify under 2% (24/3,567 or 0.7% in 2008) as newly acquired, significantly less (χ^2 $P < 0.001$) than the proportion of cases (381/11,303 or 3.4% in 2008) identified as newly acquired nationally.[12] Currently, most public health units (PHUs) in New South Wales do not identify HCV cases as newly acquired unless already reported as such on the notification form. These cases are followed up with patients' doctors by PHU staff to confirm newly acquired status and obtain enhanced surveillance data on clinical history and risk factors. A trial in 2000 of enhanced surveillance of all HCV notifications in New South Wales identified 5.7% (307/5,409) of followed-up notifications as newly acquired, but was discontinued owing to data quality and resource constraints.[13] An alternative methodology to improve identification of newly acquired HCV by the New South Wales surveillance system without increasing the burden on PHUs or being dependent on contact with multiple doctors was developed and tested. This paper presents results and compares the characteristics of newly acquired HCV cases identified from laboratory data with those reported to the NSW Department of Health (NSW Health), for the year 2007.

Methods

All laboratories in New South Wales report all HCV antibody positive test results to NSW Health via the relevant Area Health Service's PHU. Acute symptomatic cases diagnosed by physicians are also reported to local PHUs. For each notification not previously reported to a PHU, details are entered onto the New South Wales Notifiable Diseases Database (NDD).

De-identified data on HCV cases notified in 2007 were provided with permission from the Communicable Diseases Branch, NSW Health (November 2009). This study focussed on notifications during 2007 to allow adequate time for receipt of all notifications and removal of duplicates from the NDD. Cases' ages, gender and date of receipt were provided. Data were also obtained from a public laboratory (Laboratory A), which covers requests from specialists, tertiary clinics and general practitioners within one PHU catchment area, and a private laboratory (Laboratory B), which receives specimens from across the state, primarily from general practitioners.

The following laboratory data were used in the analysis: HCV antibody test records in 2007 (HCV antibody positive records only from Laboratory B); available HCV antibody test records from 2005–2007 for patients testing antibody positive in 2007; and HCV RNA test records in 2007 (Laboratory A only). Data were provided for 12,939 unique patients. Each record contained the date the specimen was received, medical record number (MRN; Laboratory A) or Patient Identification Number (PIN; Laboratory B), residential postcode, gender, date of birth (Laboratory A) or age (Laboratory B), and first and surnames of patient (Laboratory A only). Ethics approval was provided prior to commencement by the South Eastern Sydney and Illawarra Area Health Service Northern Hospital Network (08/163) and the University of New South Wales (08063) Human Research Ethics Committees.

Duplicates were removed and records deleted for patients residing outside New South Wales (n = 239) and where date of birth (n = 136) or test results (n = 151) were missing or inconclusive. Each record was assigned an area health service according to the postcode of residence. HCV RNA negative and indeterminate records from Laboratory A were discarded and the RNA positive records combined with cleaned HCV antibody test records from each laboratory. Records were linked via a combination of first name, surname, date of birth and gender (ID; Laboratory A) or the PIN (Laboratory B). No records had identical MRNs and non-identical IDs.

To identify new diagnoses of HCV in 2007, records were sorted in order of ID, date received and type of test (antibody or RNA). Records that satisfied the following criteria were identified.

a) A positive HCV antibody test result in 2007 where the earlier record did not match ID (new diagnosis). For a patient with multiple positive HCV antibody results, the record indicating a new diagnosis was taken as the earliest result.
b) A positive HCV antibody test in 2007 where the next earliest record matched ID and had a HCV antibody negative result (new diagnosis). If the HCV antibody negative test was within the preceding 24 months this was deemed a newly acquired case (Box, definition 1a).
c) A positive HCV RNA test in 2007 where the next earliest record matched ID and had a HCV antibody negative result (new diagnosis). If the antibody negative test was within the preceding 24 months this was deemed a newly acquired case (Box, definition 1b).

This process resulted in the identification of 2,207 cases of newly diagnosed HCV and 22 newly acquired cases of HCV, including 2 cases fulfilling definition 1b.

The 96 inconclusive test results were compared with newly diagnosed cases to check for combinations of test results that would invalidate the diagnosis, such as an inconclusive test prior to the positive test (with no earlier negative test); none was found. Comparison of age, gender and test dates of the newly acquired cases from each laboratory found no matches, therefore newly acquired cases identified by each laboratory were deemed unique.

The 22 newly acquired HCV cases identified from the laboratory datasets were also compared with those identified by NSW Health in 2007. Cases were linked via name code (first two letters of first and last names, Laboratory A only), postcode, gender, date of birth or age, and date of diagnosis. Earlier records were searched where cases did not match 2007 NSW Health data. In this way, 1 case was found to have been first notified to NSW Health in 1999 and was removed from the dataset. Analyses were conducted using SAS statistical software version 9.2 (SAS Institute Inc. Cary, North Carolina), STATA 10.0 (College Station, Texas) and Microsoft Excel 2007.

Results

Of the 2,206 newly diagnosed HCV cases from the laboratory datasets, 21 newly acquired cases were identified. While 17 (81%) of these cases had also been identified by NSW Health as newly diagnosed, 4 (19%) had not been previously identified (Table 1). Only 3 (14%) of our laboratory-identified

Box:

Definition of newly acquired HCV

- Laboratory definitive evidence, or
- Laboratory suggestive evidence and clinical evidence.

Laboratory definitive evidence

- Detection of anti-HCV antibody from a person who has had a negative anti-HCV antibody test recorded within the past 24 months (Definition 1a), or
- Detection of HCV by nucleic acid testing from a person who has had a negative anti-HCV antibody test result within the past 24 months (Definition 1b), or
- Detection of anti-HCV antibodies in a child aged 18 to 24 months (Definition 1c), or
- Detection of HCV by nucleic acid testing, in a child aged 1 to 24 months (Definition 1d).

Laboratory suggestive evidence

- Detection of anti-HCV antibody or HCV by nucleic acid testing.

Clinical evidence

Clinical hepatitis within the past 24 months (where other causes of acute hepatitis have been excluded) defined as:

- Jaundice, or
- Bilirubin in urine, or
- Alanine transaminase (ALT) seven times upper normal limit.

newly acquired HCV cases were identified as such by NSW Health: the remainder were categorised as newly diagnosed or were unidentified. Our examination of laboratory data from one private and one public laboratory increased the overall proportion of newly acquired HCV cases identified in 2007 in New South Wales from 1.6% (65/4,192) to 2.0% (83/4,196).

Table 2 illustrates the age and gender breakdown of laboratory– and NSW Health-identified newly acquired cases. Laboratory-identified cases (median 34 years) were older than NSW Health cases (median 28 years) although this was not statistically significant. No cases aged less than 20 years were found in the laboratory data. Laboratory-identified cases were significantly more likely than NSW Health-identified cases to be aged 30 or more years (71% vs 45%; c^2 $P = 0.033$). A recent review of the Victorian HCV surveillance system also found that laboratory follow-up identified an older sub-set of cases,[11] thus restricting follow-up to a particular age group may not be advised.

Discussion

The two laboratories selected for this trial accounted for up to half of all newly diagnosed HCV cases in

Table 1: Laboratory-identified newly acquired hepatitis C virus cases matched and unmatched to NSW Health-identified cases

	Laboratory A (n)	Laboratory B (n)	Combined n	Combined %
Laboratory-identified newly acquired HCV cases	9	12	21	100
Matched to NSW Health records				
Newly acquired	1	2	3	14
Newly diagnosed	6	8	14	67
Unmatched to NSW Health records	2	2	4	19

Table 2: Laboratory and NSW Health-identified newly acquired hepatitis C virus cases, by age and gender

	Laboratories		NSW Health	
Median age	34 years		28 years	
Age	n	%	n	%
< 30 years	6	29	36	55
≥30 years	15	71	29	45
Total	21	100	65	100
Male	15	71	36	55

New South Wales in 2007. Of the 2,206 laboratory-identified newly diagnosed cases, a total of 21 newly acquired cases of HCV infection were identified.

The comparison of these 21 cases with the 65 newly acquired HCV cases identified by NSW Health revealed that 18 had not been previously identified by NSW Health as newly acquired, bringing the total number of newly acquired HCV cases for 2007 to 83. This increased the proportion of newly acquired HCV cases for 2007 from 1.6% (65/4,192) to 2.0% (83/4,196) and increased the total yield by 28%. Laboratory follow-up also detected a significantly higher proportion of cases aged 30 years or over, probably owing to older people being less itinerant than younger people and more likely to have repeat pathology tests performed through the same laboratory. This suggests that laboratory follow-up could potentially contribute to more fully characterising newly acquired HCV cases in New South Wales.

This report has a number of limitations. Past testing history could only be reported by the laboratories where previous tests were performed by the same laboratory. No RNA data were available from Laboratory B, therefore cases fulfilling definition 1b could not be identified. For Laboratory A, HCV antibody negative records prior to 2007 were unavailable for HCV antibody negative patients in 2007. This meant newly acquired cases fulfilling definition 1b where the antibody test was conducted in 2005–2006 could not be included.

The last two limitations each potentially reduce the number of newly acquired HCV cases otherwise identifiable. 'Newly diagnosed' means only within each laboratory and thus the number identified is an overestimate; some patients may have previously tested positive through another laboratory. Name variations such as omission of middle names and alternative spellings were not taken into account when matching tests as a standard surveillance system is unlikely to be able to account for this level of detail. It is unknown if any of the 2,206 cases identified in this study as newly diagnosed in 2007 were notified by another laboratory prior to diagnosis by the laboratories in this study. This would affect the date and possibly the year of diagnosis. However, as most laboratory-identified newly acquired HCV cases identified were matched to NSW Health newly diagnosed cases (17/21), and a search for earlier notification dates for the 4 unmatched cases was unsuccessful, this appears unlikely for newly acquired cases identified here. The NDD is expected to be complete for new HCV diagnoses.

While our results indicate 4 of the 21 (19%) newly acquired HCV cases identified from the laboratory datasets were not recorded in the NDD, it is possible these cases were diagnosed at another laboratory where name code and/or date of birth were recorded differently or erroneously. Data linkage between the two laboratories was not possible and is not currently performed by NSW Health. However our results suggest that linkage between two or three large laboratories could potentially significantly increase identification of newly acquired HCV.

Implications

The 28% increase in the number of newly acquired HCV cases identified by this study indicates that, used in conjunction with current reporting mechanisms, laboratory data have the potential to increase both the proportion and the yield of newly acquired cases in New South Wales without requiring contact with multiple doctors for test results. Linkage to laboratory data may also be likely to enhance the identification of newly acquired cases among older people. HCV notifications data for 2008 reveal that the number of newly acquired cases identified in New South Wales dropped to 24/3,916 (0.6%)[14] as one area health service ceased follow up of all HCV notifications. If this trend continues, laboratory data could be even more important in improving the surveillance system for newly acquired HCV cases in New South Wales. A more comprehensive prospective study should be undertaken to determine the likely extent of improvements.

Acknowledgements

We thank staff from the laboratories for data provision. This study was funded by the NSW

Department of Health. Lisa Maher is supported by an NHMRC Senior Research Fellowship. The National Centre in HIV Epidemiology and Clinical Research is funded by the Australian Government Department of Health and Ageing, and is affiliated with the Faculty of Medicine, The University of New South Wales. The National Centre in HIV Social Research is funded by the Australian Government Department of Health and Ageing, and is affiliated with the Faculty of Arts and Social Sciences, The University of New South Wales. The views expressed in this publication do not necessarily represent the position of the Australian Government.

Author details

Dr Rachel M Deacon, Research Coordinator, Viral Hepatitis Epidemiology and Prevention Program[1]
Dr Handan Wand, Senior Lecturer, Biostatistics and Databases Program[1]
Dr Sacha Stelzer-Braid, Postdoctoral Scientist, Virology Research[2]
Associate Professor Carla Treloar, Head, Hepatitis C Research Program and Deputy Director[3]
Professor Lisa Maher, Head, Viral Hepatitis Epidemiology and Prevention Program[1]

1. National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, Sydney, New South Wales
2. Department of Microbiology, South Eastern Area Laboratory Service, Prince of Wales Hospital, Randwick, New South Wales
3. National Centre in HIV Social Research, University of New South Wales, Sydney, New South Wales

Corresponding author: Dr Rachel M Deacon, Research Coordinator, Viral Hepatitis Epidemiology and Prevention Program, National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, SYDNEY NSW 2052. Telephone: +61 2 9385 0935. Facsimile: +61 2 9385 0920. Email: Rdeacon@nchecr.unsw.edu.au

References

1. Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. *Lancet Infect Dis* 2005;5(9):558–567.
2. Sy T, Jamal MM. Epidemiology of hepatitis C virus (HCV) infection. *Int J Med Sci* 2006;3(2):41–46.
3. NNDSS Annual Report Writing Group. Australia's notifiable disease status 2008: Annual report of the National Notifiable Diseases Surveillance System. *Commun Dis Intell* 2010;34(3):157–224.
4. Guy R, Devadason D, Lim M, Higgins N, Pedrana A, Gibson K, et al. Enhanced case detection for newly acquired hepatitis C infection: epidemiological findings and health service implications. *Commun Dis Intell* 2008;32:250–256.
5. Robotin MC, Copland J, Tallis G, Coleman D, Giele C, Carter L, et al. Surveillance for newly acquired hepatitis C in Australia. *J Gastroenterol Hepatol* 2004;19(3):283–288.
6. Spencer J, Dore G, Robotin M, Correll P, Kaldor J, Communicable Diseases Network Australia Viral Hepatitis Surveillance Committee. Outcomes from the first two years of the Australian hepatitis C surveillance strategy. *Commun Dis Intell* 2002;26(1):14–22.
7. Corey KE, Mendez-Navarro J, Gorospe EC, Zheng H, Chung RT. Early treatment improves outcomes in acute hepatitis C virus infection: a meta-analysis. *J Viral Hepat* 2010;17(3):201–207.
8. Begg K, Roche P, Owen R, Liu C, Kaczmarek M, Hii A, et al. Australia's notifiable diseases status, 2006: Annual report of the National Notifiable Diseases Surveillance System. *Commun Dis Intell* 2008;32(2):139–207.
9. Roy KM, Goldberg D, Taylor A, Mills P. Investigating the source of hepatitis C virus infection among individuals whose route of infection is undefined: a study of ten cases. *Scand J Infect Dis* 2003;35(5):326–328.
10. Department of Human Services Victoria. Notifications of infectious diseases. Victorian Summary Report 1 January to 9 December 2008. Melbourne: Communicable Disease Control, Public Health Branch, Department of Human Services Victoria; 2008.
11. Department of Human Services Victoria. The effectiveness of intensive laboratory follow up for hepatitis C infections in Victoria, January to March 2006. Melbourne: Communicable Disease Control, Public Health Branch, Department of Human Services Victoria; 2006.
12. National Centre in HIV Epidemiology and Clinical Research. HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report 2009. National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, Sydney, NSW.
13. NSW Department of Health. Evaluation of the enhanced hepatitis C surveillance system in NSW 2001. Sydney: NSW Department of Health; 2002.
14. Communicable Diseases Branch, NSW Department of Health. Year in review: communicable disease surveillance, NSW, 2008. *NSW Public Health Bulletin* 2009;20(9–10):141–151.