Research Article

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Hospital-related morbidity in people notified with hepatitis C: A population-based record linkage study in New South Wales, Australia

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Background & Aims: Statistics are available about hepatitis C (HCV)-related transplants, mortality and cancer risk but little is known about morbidity in the earlier stages of infection. We examined condition specific (principal diagnosis) and overall hospitalization rates for the cohort of individuals notified with hepatitis C in New South Wales (NSW), Australia.

Methods: HCV notifications in NSW were linked to their hospital records (available for July 2000 to June 2006), HIV and hepatitis B notifications, and death records. Cases co-infected with HIV or hepatitis B were excluded. Hospitalization rates by person-years of observation were calculated and compared with those expected using rates for the NSW population to calculate standardized hospitalization ratios (SHRs).

Results: Patterns of admission were generally similar to the NSW population, with the highest rates in the elderly. However, rates were 42% higher than expected overall and significantly increased in ages 15–64 years. The greatest was excess in 15–19 year olds (SHR 3.8, 95% CI 3.4–4.2), especially females (SHR 4.5, 95% CI 4.1–4.9). Lifestyle factors accounted for the highest absolute and relative rates in young adults while liver disease contributed the greatest burden in older adults. Illicit drug-related conditions accounted for 9% of admissions (SHR 16.1, 95% CI 15.7–16.6) while alcohol and liver-related conditions each accounted for 5% (SHRs 5.1, 95% CI 4.9–5.4 and 15.7, 95% CI 15.0–16.4, respectively).

Conclusions: Our findings highlight the need for strategies to minimize lifestyle-related harms, including alcohol consumption, and to improve HCV treatment uptake, in order to reduce morbidity in people with HCV infection.

Keywords: Hepatitis C; Record linkage; Epidemiology; Morbidity; Hospitalization.

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Abbreviations: HCV, hepatitis C virus; NSW, New South Wales; NDD, Notifiable Diseases Database; NHD, National HIV Data Base; NAR, National AIDS Registry; ICD-10-AM, 10th revision of the International Classification of Diseases–Australian Modification; CHeReL, Centre for Health Record Linkage; SHR, standardized hospitalization ratio; CI, confidence interval; IDU, injecting drug user; SMR, standardized mortality ratio.

Introduction

Infection with the hepatitis C virus (HCV) is associated with increased morbidity and mortality. Previous studies have reported a 3- to 5.5-fold increased risk of death and a higher incidence of liver cancer and immunoproliferative malignancies [1–6]. HCV is also now the most commonly reported primary indication for liver transplant in many industrialised countries including Australia [7,8]. However, the burden of morbidity associated with the earlier stages of HCV infection, at a population level, is not well studied.

HCV-associated hospital admissions have been described using population-based registers [9–11], and rates of hospitalization have been reported for specific HCV infected cohorts [12,13]. However, we know of only one other published study examining population-based hospitalization rates; in 469 HCV cases notified in Scotland [14]. Here, we report hospitalization rates for all individuals notified with HCV in New South Wales (NSW), Australia and compare them with those expected using rates for the NSW population.

Methods

Data sources

By law all new hepatitis B and C and HIV diagnoses are notifiable in Australia by the diagnosing laboratory and/or clinician. Our study cohort included all people notified with HCV mono-infection recorded on the NSW Notifiable Diseases Database (NDD) between 1992 (when personal identifiers were first recorded) and 2006. HCV cases co-infected with HIV and HBV were excluded as we wanted to specifically examine hospital-related morbidity associated with HCV infection and co-infected cases were expected to have a different pattern of hospitalization. Co-infected cases were identified by linkage to NDD notifications for hepatitis B and to NSW data from the National HIV Data Base (NHD) and National AIDS

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Registry (NAR). HIV infections have been notifiable in NSW since 1985 and the NAR contains data on all AIDS diagnoses since 1982. The NDD, NHD, and NAR records contain demographic information (including full name for NDD and name code [first two letters of surname and given name] for HIV and AIDS notifications) and variables for disease code and diagnosis date (date of laboratory test request).

The Admitted Patient Data Collection ('hospital data') covers all inpatient admissions from all public (including psychiatric) and private hospitals in NSW. The data are collected by financial year (1 July to 30 June) of separation (discharge, transfer, death, or change in admission type within the same hospital). Each admission includes demographic and administrative information and diagnosis and procedure fields coded according to the 10th revision of the International Classification of Diseases–Australian Modification (ICD-10-AM). Up to 55 diagnostic codes can be recorded for each admission, with the principal (first) diagnostic code used to record the main condition responsible for the admission. Patient name has been recorded since 1 July 2000. For this reason, the analysis was limited to separations from 1 July 2000 to 30 June 2006 (the most recent year data were available).

The Registry of Births Deaths and Marriages is a registry of all deaths (based on receipt of a medical certificate of cause of death) in NSW and includes the date of death. We used date of death to determine if and when a person died in order to censor their person-years of observation.

Linkage process

Data linkage was carried out by the Centre for Health Record Linkage (CHeReL) [15]. The NDD, hospitalization and death data were linked using probabilistic record linkage methods and *ChoiceMaker* software [16]. Full name on the NDD data set was then recoded to name code before linkage with the AIDS/HIV registries using deterministic methods based on a 100% match on name code, date of birth, and sex.

Analysis

The study period was defined as 1 July 2000–30 June 2006. Cases were defined as ineligible if they died before the start of the study period or within 14 days of their HCV diagnosis date, or were diagnosed within 14 days of the end, or after, the study period. Eligible cases were also excluded if age or sex were missing. All hospital admissions in the cohort before or beginning within 14 days of diagnosis were excluded to reduce the bias towards higher rates of admission around the time of diagnosis [6]. In both the cohort and NSW population, duplicate and nested admissions (i.e. an admission within the date range of another admission) were removed such that there was only one principal diagnostic code for each time period. In addition, because of the extremely high frequency of admissions with a principal diagnostic code of extracorporeal dialysis (Z49.1) we decided to exclude them from the analysis. The number of remaining admissions was categorized by their principal diagnostic code.

Rates of admission were calculated using person-years at risk as the denominator. This was calculated for each person as the time 14 days after diagnosis or from the start of the study period (whichever was later) until the end of the study period or death (whichever came first). Numbers of admissions were compared with those expected using rates for the NSW population by 5 year age group, sex and calendar year of hospitalization to calculate standardized hospitalization ratios (SHRs). The population of NSW is 7 million, of which approximately two-thirds live in the capital city, Sydney, and one-third were born overseas. To account for the correlation between hospitalizations for the same person, a random effects Poisson regression model [17] was used to examine trends in rates over time, and 95% confidence intervals (CIs) for SHRs were calculated using the method by Stukel et al. [18].

Ethics approval

Ethics approval was granted by the University of NSW and the NSW Population and Health Services Research Ethics Committee.

Results

Study cohort

There were 91,986 people notified with HCV in 1992–2006; 4731 (5.1%) were ineligible and 754 (0.9%) of those eligible were missing age or sex. Of the remaining cohort (n = 86,501), 3217 (3.7%) had HBV co-infection, 683 (0.8%) had HIV co-infection and 38 (0.04%) had both HIV and HBV co-infection leaving 82,601 people with HCV mono-infection for analysis (Table 1). After exclusion of admissions for extracorporeal dialysis (17% and 9.1% of admissions in the HCV cohort and NSW population, respectively), and then admissions that occurred at the time of or within 14 days of the HCV diagnosis date (2.7% of admissions in the HCV cohort), the most commonly recorded principal diagnosis was 'Mental and behavioral disorders due to use of opioids, dependence syndrome' for the HCV cohort (3.2%) and 'Singleton, born in hospital' for the NSW population (2.5%).

All conditions

Of admissions in the NSW population, 1.2% were in the HCV mono-infection cohort, which experienced admission rates 42% higher than expected (Table 2). Crudes rates were 30% higher in females than males, but SHRs were higher in males (1.51, 95% CI 1.49–1.53) than females (1.33, 95% CI 1.31–1.35). As with the NSW population, admission rates increased with age after 40–44 years (Fig. 1). Admission rates were significantly higher than expected in ages 15–64 years with the greatest excess in 15–19 year olds (SHR 3.8, 95% CI 3.4–4.2), especially females (SHR 4.5, 95% CI 4.1–4.9).

Illicit drug use

Mental and behavioral disorders accounted for 24% of all admissions in the cohort (compared with 4.6% in the NSW population) and had the highest rates of any chapter (Table 2). Thirty-seven percent of these admissions were directly related to illicit drug use, with rates 16-fold higher than expected (Table 3). As with trends for the NSW population, rates peaked in young adults and at an earlier age in females than males (Fig. 2). However, in the HCV cohort, the peak was considerably higher, at an earlier age and in females rather than males. Therefore SHRs were significantly raised in all age/sex groups and significantly higher in females than males in all age groups under 50 years.

HCV hepatitis and associated liver diseases

HCV hepatitis-related admissions had the highest rates within the liver disease group (Table 3), contributing 1.9% of all admissions and 65% of the Infection chapter group (Table 2). Although most of the additional burden from infection was due to HCV-related admissions, the rate for non-HCV-related infections was also significantly higher than expected (SHR 1.4, 95% CI 1.3–1.5). Of the HCV hepatitis-related admissions, 4% were for acute and 96% for chronic hepatitis. Rates generally increased with age, peaking in the 60–69 year age group (Fig. 3).

Table 1. Description of HCV mono-infection cohort.

Number of unique people	82,601
Median age at entry into study (interquartile range)	37 (29–44)
Males *N* (%)	52,016 (63)
Diagnosed during study period *N* (%)	31,221 (38)
Linked to hospital records *N* (%)	33,152 (40)
Linked to deaths *N* (%)	2844 (3)
Total person-years f/up	40,4471
Mean person-years f/up per person	4.9