Full analysis of comorbidities in chronic hepatitis C patients compared with matched comparators: a nationwide population-based register study from 2001 to 2013

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ABSTRACT

Patients with chronic hepatitis C (CHC) virus infection have an increased risk of comorbidities (Lavrão et al. 2012). In Sweden, the International Classification of Diseases, 10th revision (ICD-10) has been used since 1997 for recording diagnoses in the patient register (Socialstyrelsen 2018). However, in order to make the analysis of comorbidities easier and more relevant for capturing the extra-hepatic manifestations of CHC, most previous studies have grouped morbidity diagnoses into larger groups, often using comorbidity indices such as the Charlson comorbidity index or the HepC(8) (Buch et al. 2017, Anmpuero et al. 2018). In the present study, we analyzed the risk of comorbidities in patients with CHC compared to ICD-10 diagnoses.

METHODS

In Sweden, universal access to health-care is provided to the population through a tax-funded system. Patients with CHC are typically cared for by specialists in infectious diseases or gastroenterology in hospital-based outpatient clinics or inpatient facilities. They are not managed by general practitioners in primary care (Buch et al. 2017).

DATA SOURCES

The National Patient Register (Table 1), kept by the Swedish National Board of Health, uses the Swedish adaptation of the ICD-10 called ICD-10-Socialstyrelsen 2018). Patients with CHC were identified using the ICD-10 called B18.2. Data on date of residence, vital statistics, and emigration status were retrieved from the Register of the Total Population held by Statistics Sweden (up to December 31, 2012). This register covers the entire Swedish population and includes information on age, sex, and place of residence, as well as dates of birth, death, and emigration status. Information regarding death was retrieved from the Cause of Death Registry. The Swedish personal identity number (social security number) was used to link individuals between registers.

Up to five general population comparators were matched by age, sex, and county of residence to each patient at time of diagnosis. The study was approved by the Regional Ethics Committee, Karolinska University Hospital, Stockholm, Sweden.

STATISTICAL METHODS

Data handling was conducted using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA) and data analyses were performed using Excel (version 14; Microsoft, Seattle, WA, USA). The standardized incidence ratios (SIRs) were calculated as the ratio of the observed number of patients to the expected number, which was calculated using the age- and sex-specific incidence rates of the reference population. The method used was the direct method, with standardization for age groups. The SIR was used as the measure of relative risk, and was expressed using SIRs (95% CI).

RESULTS

The CHC cohort (n=24,522) was followed for 281,623 person-years (mean 11.5 years) and the comparator cohort (n=202,940) was followed for 1,764,765 person-years (mean 7.4 years). One-third of the patients were men.

Risk for individual ICD-10 diagnoses

The ICD-10 contained 2,213 diagnoses. The lower 95% CI did not cross 1 for 69% of the diagnoses (n=1,222; data not shown), suggesting that patients with CHC to be at an increased risk for these diagnoses. The 27 diagnoses in which patients with CHC were at the highest risk are shown in Fig 1A. The highest risk was in the category “Other acute viral hepatitis” (B17.1; SIR, 2.53; 95% CI, 2.48-2.58). Patients with CHC were at a lower risk for the upper 95% CI did not cross 1 for 12% of the diagnoses (n=27; Fig 1B). The diagnosis with the lowest risk for CHC patients was multiple sclerosis (G35; SIR, 0.37; 95% CI, 0.26-0.50), which is described in more detail in post. By analyzing the risk of CHC patients compared with matched comparators: a nationwide population-based register study from 2001 to 2013.

DISCUSSION

In the present study, patients with CHC were at a higher risk for the majority of diagnoses. The highest risks were seen for other viral hepatitis diagnoses, mental and behavioral disorders, and diagnoses associated with a need for blood products, or diagnoses due CHC sequelea or a consequence of a more herculean style life. By analyzing the risk using the by WHO predefined grouped ICD-10 diagnoses, these patients were at a higher risk for all grouped diagnoses within ICD-10 chapters I (blood diseases), IV (metabolic diseases), V (mental disorders), II (respiratory system diseases), III (diabetes mellitus), X (infectious/parasitic diseases), X (diseases of musculoskeletal system and connective tissue), XI (perinatal conditions), XVIII (other symptoms), XIX (external injury and poisoning), and XXI (health service contacts).

However, the patients with CHC were at a lower risk for neoplasms in male genital organs (C60–C62), dematoolgous diseases of the central nervous system (G30–G34), glaucoma (H40–H44), and radiation-related disorders of the ear (N82–N84). The National Patient Register does not contain any data from pharmacies, IPD, any hospitals, or any diagnoses that mostly received care outside of hospitals could have been underestimated. The study did not include any sensitivity analysis to, for example, avoid surveillance bias due to increased surveillance among people with diagnosed patients with CHC. Also, the analyses were not adjusted for multiple comparisons.

CONCLUSIONS

• Patients with CHC were at a higher risk for the majority diagnoses. The highest risks were due to risk behaviors patients, mental disorders, disease sequelea, or receiving blood products.
• The patients were at a lower risk for a few diagnoses such as MS, Diabetes mellitus, glaucoma, prostate neoplasm, and skin changes.

Fig 1. Highest 27 (A) and lowest 27 (B) Standardized Incidence Ratios (95% CI) for patients with CHC.

REFERENCES


Fig 2. Standardized Incidence Ratios (95% CIs) for Patients with CHC: 95% CI Over (Accessed www.socialstyrelsen.se/klassificeringochkoder/diagnoskodericd 2012;12:86. Socialstyrelsen 2018. Available at: www.socialstyrelsen.se/klassificeringochkoder/diagnoskodericd

Table 1. Description of the National Patient Register

<table>
<thead>
<tr>
<th>Diagnosis Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHC</td>
<td>Chronic hepatitis C</td>
</tr>
<tr>
<td>T2D</td>
<td>Type 2 diabetes</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>MS</td>
<td>Multiple sclerosis</td>
</tr>
</tbody>
</table>

ABBRIVATIONS

ATC - Anatomical Therapeutic Chemical; CI – confidence interval; CHC – chronic hepatitis C; IC – International Classification of Diseases; MS – multiple sclerosis; SIR – standardized incidence ratio