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Epidemiology of hepatitis B infection in Finland: Implications for immunisation policy

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ABSTRACT

Objectives: We describe the current epidemiology of acute and chronic hepatitis B infections in Finland. We estimate the total incidence of chronic hepatitis B following from the current incidence of acute infections and the influx of chronic carriers of hepatitis B associated with net immigration. We evaluate the incidence of hepatitis B infections preventable by a universal vaccination programme among infants.
Methods: We analysed hepatitis B cases reported to the National Infectious Disease Register during 2004–2012 and used pre-developed methods to adjust for acute asymptomatic infections. We estimated the projected incidence of chronic infection by applying age-specific risks of chronic infection to the estimated incidence of acute infection. We estimated the influx of chronic carriers associated with immigration by utilising data on immigration during 2004–2012 and the WHO regional estimates of carriage prevalence.
Results: The estimated incidence of acute hepatitis B infection in Finland, adjusted for asymptomatic infections, was 1.67 per 100,000 per year (95% CrI 1.43–1.94) which is 4.2-fold to the register-based incidence. The estimated lifetime risks of acute and chronic hepatitis B infections were 0.13% and 0.01%, respectively. We estimated that annually seven new chronic infections would result from infections acquired in Finland. These new chronic infections accounted for 1.2% of the total incidence of chronic infections. We estimated that eventually three chronic infections per year would be potentially preventable by a universal infant vaccination programme.
Conclusions: Partly due to the fact that hepatitis B infections in neonates and in children are rare, a very limited number of chronic hepatitis B infections resulted from infection acquired within the country. A vast majority of chronic hepatitis B infections occurred among foreign-born persons and were therefore not preventable by a universal infant immunisation programme in Finland. Even with a targeted immunisation programme, the incidence of hepatitis B infection has remained low.

1. Introduction

Initial infection with hepatitis B virus (HBV) may remain subclinical or cause acute self-limited hepatitis and, in rare occasions, fulminant hepatitis progressing to liver failure [1,2]. Infected individuals may develop chronic infection which can lead to cirrhosis or hepatocellular carcinoma. The clinical picture of acute hepatitis and the proportion of infected developing chronic infection are age-dependent. Over 90% of perinatal infections remain asymptomatic. However, infected infants have the highest risk of developing chronic infection [1,3,4].

Persistence of hepatitis B surface antigen (HBsAg) is the principal marker of chronic infection [3]. The prevalence of HBV infection varies geographically from high (⩾8%), high intermediate (5–7%), low intermediate (2–4%), low (<2%) to very low (<0.5%) [5–8]. Global estimates of the number of people with chronic infection vary from 240 to 360 million [6,7,9].

WHO recommends incorporating universal hepatitis B vaccination into national infant immunisation programmes [9]. However, the hepatitis B vaccination programmes in several northern European countries (i.e. Denmark, Finland, Iceland, Norway, Sweden and the United Kingdom) have targeted risk groups only [10,11]. These countries have very low HBV infection prevalence [8,12] and most new hepatitis B infections are acquired by young adults sexually or through injecting drug use [1].

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Finland's national hepatitis B vaccination programme started in 1993. Up to 2015, the programme targeted close contacts of hepatitis B infected individuals, patients with bleeding disorders, injecting drug users with their close contacts, sex workers and certain student groups. The vaccine coverage in all of these risk groups is not well known, but among injecting drug users the coverage of at least one dose of hepatitis B vaccine is 40–65% [13–15]. In addition, all pregnant women and blood donors are routinely screened for HBsAg. Also refugees and asylum seekers from countries with HBV infection prevalence higher than 2% are offered screening [16].

In this study we describe the current epidemiology of acute and chronic hepatitis B infections in Finland. We estimate the projected incidence of chronic hepatitis B following from the current incidence of acute infections and the influx of chronic carriers of hepatitis B associated with net immigration. Based on this we also evaluate the incidence of hepatitis B infections preventable by a universal vaccination programme among infants in a country with very low HBV infection prevalence.

2. Methods

2.1. Data and case definitions

In Finland, hepatitis B infections are notified to the National Infectious Disease Register (NIDR) by both physicians and licensed clinical microbiological laboratories. Notification is mandatory by the Communicable Disease Act (583/86) and the Communicable Disease Decree (786/86). Only microbiologically confirmed hepatitis B infections are registered. Separate notifications within 50 years concerning the same person are combined to a single case using the personal identity code (ID). Other identification information (name, gender, date of birth) is used if the person's ID is missing or incomplete. The physician reports complement the laboratory findings with more extensive details, including the assumed route of transmission and the clinical diagnosis of hepatitis B infection. The NIDR data are routinely augmented with additional information (place of residence, date of death, country of birth, most recent nationality) retrieved from the Population Register Centre.

Cases reported to NIDR between 1 January 2004 and 31 December 2012, were included in the analyses. A case of acute hepatitis B was defined as one with a positive laboratory finding of IgM antibodies (S-HBc-AbM). All other hepatitis B cases were defined as chronic.

2.2. Estimation of the true incidence of acute infection

The incidence of acute hepatitis B was first estimated based on the numbers of registered acute cases in NIDR. These cases were assumed to be symptomatic. The true incidence of acute hepatitis B infection, including asymptomatic infections, was calculated by dividing the register-based incidence by an earlier-derived age-dependent proportion of infections which are symptomatic [17,18].

2.3. Estimation of the projected incidence of chronic infection

A projected incidence of chronic hepatitis B infection following acute infection was derived from the estimated true incidence of acute hepatitis B infection. For infections acquired under 1 and over 32 years of age, 88.5% [3] and 4.0% [4,17] risks of developing chronic infection were assumed, respectively. For infections acquired between those ages, a function describing the age-dependent proportion of acute hepatitis leading to chronic infection was used [4,17].

2.4. Persons immigrating with chronic hepatitis B infection

Data on immigration to Finland during 2004–2012, stratified by country of birth, gender and age (Statistics Finland), were multiplied by the corresponding proportions of chronic carriers in the region using year 2005 estimates [6] to derive predictions about the annual average of number of foreign-born persons immigrating with chronic hepatitis B infection.

2.5. Vaccination scenario and preventable hepatitis B infections

We estimated the annual numbers of potentially preventable infections in a universal hepatitis B vaccination programme among infants. Vaccine efficacy and immunisation coverage were both assumed to be 100%. No herd effect was considered. The reduction in the incidence due to vaccination applies only to individuals born in Finland who are one year old or older.

2.6. Statistical analysis

Analyses were performed using the Stata 14.0 and R softwares (version 3.1.3). The incidence rates of hepatitis B infection were estimated as Bayesian posterior distributions, based on the Poisson likelihood and uninformative priors on the rate parameters in 5 year age-bands. Population-level estimates were calculated as age-standardised rates. The estimated incidence rates are presented as posterior mean estimates and 95% equitail posterior intervals (credible intervals, CrI).

2.7. Ethical approval

The study plan was approved by the Research Ethics Committee of the National Institute for Health and Welfare (meeting protocol 5/2013 § 569).

3. Results

3.1. Acute hepatitis B

3.1.1. Age, gender, and demographics

The incidence of acute hepatitis B during the study period (2004–2012) was stable and low (Fig. 1). The average number of registered acute cases during 2004–2012 was 21 cases per year (range 17–30), corresponding to 0.40 per 100,000 per year (95% CrI 0.34–0.46).

Of all reported acute hepatitis B cases, 67% (N = 128) were males (Table 1). The median age of acute cases was 37 years (range 11–84) among males and 26 years (range 0–85) among females. The register-based incidence was highest among males aged 20–39 years (1.21 cases per 100,000 per year, 95% CrI 0.95–1.50) and females aged 20–24 years (0.83 cases per 100,000 per year, 95% CrI 0.43–1.35) (Fig. 2).

Overall, 35% (66/191) of the acute hepatitis B cases were foreign-born. In this group, the country of acquisition was reported for 52% of cases (34/66) and was predominantly outside Finland (88%, 30/34). Among the 125 Finnish-born acute cases, the country of acquisition was reported for 62% (77/125), and a third (27/77) of these infections had been acquired abroad. The male-to-female ratio was higher among the Finnish-born cases compared to the foreign-born cases (2.1:1.0 vs. 1.6:1.0).

3.1.2. Route of transmission

The route of transmission was reported for 44% (84/191) of the acute hepatitis B cases (Table 1). Sexual contact was the most commonly reported transmission route with 77% (44/57) among males

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