Vaccine 35 (2017) 412–418

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

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

Tanja Karvonen [a,*], Kari Auranen [a,b], Markku Kuusi [c], Tuija Leino [a]

[a] Department of Health Protection, National Institute for Health and Welfare, P.O. Box 30, FI-00271 Helsinki, Finland
[b] Department of Mathematics and Statistics, University of Turku, FI-20014, Finland
[c] Department of Infectious Diseases, National Institute for Health and Welfare, P.O. Box 30, FI-00271 Helsinki, Finland

ARTICLE INFO

Article history:
Received 20 September 2016
Received in revised form 27 November 2016
Accepted 28 November 2016
Available online 18 December 2016

Keywords:
Epidemiology
Hepatitis B
HBV
Vaccination
Immunisation

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.
© 2016 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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].

* Corresponding author.
E-mail addresses: tanja.karvonen@thl.fi (T. Karvonen), kari.auranen@thl.fi (K. Auranen), markku.kuusi@thl.fi (M. Kuusi), tuija.leino@thl.fi (T. Leino).

http://dx.doi.org/10.1016/j.vaccine.2016.11.090
0264-410X/© 2016 The Authors. Published by Elsevier Ltd.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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

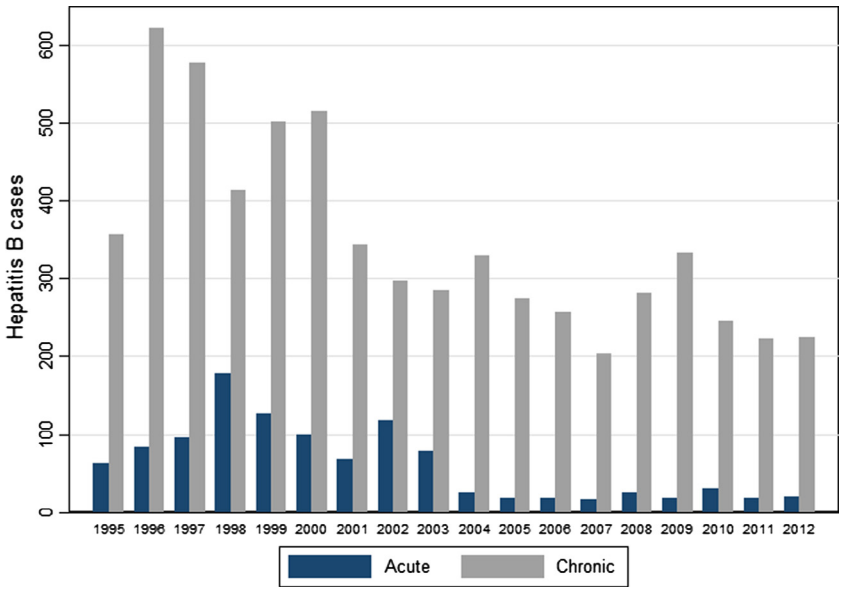

Fig. 1. The numbers of acute and chronic hepatitis B cases registered in the National Infectious Disease Register (NIDR) in Finland during 1995–2012. The analysis in this paper is based on the data from the years 2004–2012. The data from the years 1995–2003 are shown for comparison.

and 56% (15/27) among females. Finnish-born males with sexual contact as the reported route of transmission had acquired the infection mostly in Finland (15/36) or Thailand (14/36).

Intravenous drug use was reported as the route of transmission in 13% (11/84) of acute cases. Almost all (9/11) were also registered as hepatitis C positive (HCV) in NIDR. In addition, there were 17 hepatitis B cases with a registered HCV infection and in all except one case the information on the route of transmission was missing. During the last 4 years of the study period (2009–2012), only one acute case was reported with intravenous drug use as the route of transmission.

Information on the route of transmission was missing for 77% (51/66) of foreign-born acute cases. However, 45% (23/51) of these cases had information on the country of acquisition and in 91% (21/23) it was outside Finland.

3.1.3. Childhood infection

During the study period, only 4 acute hepatitis B cases were children aged less than 12 years (Table 2). Of these, one infant (<1 year old) had been born in Finland to a foreign-born mother who had chronic hepatitis B infection. The three other children ($\geqslant$1 year olds) were foreign-born. Teenagers (12–17 years) contributed to 5% (9/191) of the acute hepatitis B cases. Of the seven female teenage cases, three were foreign-born as were the two male cases. The route of transmission was known for only four teenage cases and it was then sexual contact.

3.2. The estimated true incidence of acute hepatitis B infection

The estimated true 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). The estimated incidence was thus 4.2-fold compared to the register-based data. The estimated cumulative risk of infection by 40 years of age was 0.11% and the lifetime risk 0.13%.

The estimated incidence of acute infection peaked at 20–24 year olds (5.92 per 100,000 per year, 95% CrI 4.02–8.18), which is 5.7 times higher than the register-based incidence (Fig. 2). Relative to the register-based data, the estimated incidence of acute infection was more than ten times higher among <1 year old and 1–11 years old (2.68 and 0.55 per 100,000 per year, respectively). However, the uncertainty intervals are wide in these age groups due to the very small numbers of registered cases.

3.3. Estimated incidence of chronic hepatitis B infection

We calculated that annually seven new chronic infections (66/9 = 7, Table 2) would result from the estimated incidence of acute infections. The corresponding lifetime risk of chronic infection in Finland would thus be 0.01%.

3.4. Preventable hepatitis B infections

We estimated that 58% of acute infections would be potentially preventable, i.e., acquired in Finland by a universal infant vaccination programme, corresponding to 51 (=460/9) acute infections per year (Table 2). This amounts to eventually preventing 3 (=25/9) chronic infections per year.

3.5. Chronic hepatitis B cases

The average annual number of registered chronic hepatitis B cases during 2004–2012 was 264 (range 204–334), corresponding to 4.96 cases per 100,000 per year (range 3.85–6.30, 95% CrI 4.76–5.16). The register-based acute-to-chronic ratio was thus 1:12 (Fig. 1).

The median age of chronic cases was similar among males (31 years, range 0–87) and females (30 years, range 0–91). Of the Finnish-born individuals, 20–34 and 50–64 year olds had the highest notification rate of chronic hepatitis B (Fig. 3).

The majority of chronic cases (82%) were registered among foreign-born individuals (Table 1). The proportion of foreign-born individuals was higher among 18–39 year olds compared to those chronic cases aged 40 years or more (90% vs. 60%) (Table 2). Other than Finnish-born individuals notified to the register were mostly 15–34 years old (Fig. 4).

The country where the infection was acquired was reported for 60% of the foreign-born chronic cases. Of these, only 2% were infected in Finland. Among the Finnish-born cases with information on the country of acquisition, 68% (89/131) were infected in Finland.

Table 1
Characteristics of acute and chronic hepatitis B cases in Finland 2004–2012.

Characteristic	Acute infection N = 191 (100%)	Chronic infection N = 2377 (100%)
Age (years)		
Median	32	31
Mean	36	33
Std.dev.	15	15
Range	0–85	0–91
Gender		
Male	128 (67.0%)	1421 (59.8%)
Female	63 (33.0%)	956 (40.2%)
Route of transmission[a]		
Sexual contact	59 (30.9%)	129 (5.4%)
Intravenous drugs	11 (5.8%)	46 (1.9%)
Other	11 (5.8%)	59 (2.5%)
Blood products	2 (1.0%)	43 (1.8%)
Perinatal	1 (0.5%)	89 (3.7%)
Unknown	82 (42.9%)	1498 (63.0%)
Not reported	25 (13.1%)	518 (21.7%)
Family history[b]		
Yes	3	115
No	167	1253
Unknown	10	501
NA	11	508
Hepatitis B/Hepatitis C co-infection[c]		
Yes	26	79
No	154	1790
NA	11	508
Country of birth		
Finland	125 (65.45%)	402 (16.9%)
Other[d]	66 (34.55%)	1938 (81.5)
NA	0	37 (1.6%)
Country of acquisition		
1. Most reported	Finland 54 (28.3%)	Somalia 164 (6.9%)
2. "	Thailand 18 (9.4%)	Russia 127 (5.4%)
3. "	Russia 6 (3.1%)	Finland 110 (4.6%)
4. "	Vietnam 3 (1.6%)	Thailand 97 (4.1%)
Not reported	80 (41.9%)	1076 (45.3%)

Abbreviation: NA, not available.
[a] Notifications may have more than one route of transmission.
[b] Including acute (N = 180) and chronic (N = 1869) hepatitis B cases with a valid ID who had at least one parent or child registered in NIDR 1995–2012 as hepatitis B cases.
[c] The proportions of hepatitis B infections 2004–2012 per hepatitis C infections registered in NIDR 1995–2012 were calculated only for valid IDs.
[d] Including acute (N = 6) and chronic (N = 356) hepatitis B cases with foreign names but missing country of birth information.

3.6. Chronic carriers of hepatitis B associated with immigration

During 2004–2012, the average annual immigration of foreign-born individuals to Finland was 18,700. According to the WHO estimates of the prevalence of hepatitis B infection by region [6], this corresponds to 3.7% of immigrants being chronic carriers. The average annual net immigration, calculated as the difference between foreign-born individuals immigrating to and emigrating from Finland, was 14,400. The corresponding number of immigrating carriers is 563 per year (Table 3). Chronic hepatitis B infections resulting from acute infections acquired in Finland (N = 7) are therefore estimated to account for only 1.2% of the total incidence of chronic infections ((7/(7 + 563)) × 100).

In theory, if screened, every new hepatitis B positive chronic carrier immigrating to Finland would be registered in NIDR. According to our results, the average annual number of registered chronic hepatitis B cases among foreign-born individuals during 2004–2012 corresponded to 31% ((1938/9/691) × 100) of the estimated number of carriers immigrating to Finland each year. In other words, more than two thirds of immigrating carriers would escape adequate diagnostics and possible treatment.

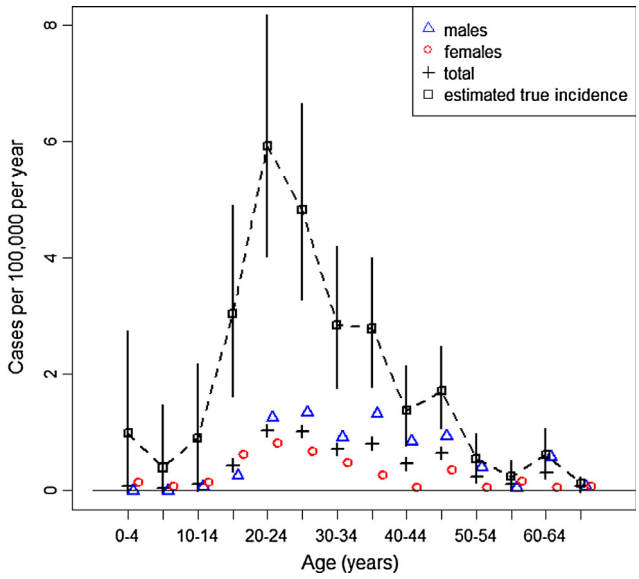

Fig. 2. Age-specific incidence of acute hepatitis B in Finland in 2004–2012. The observed incidence in 5-year age bands is based on the registered cases of acute hepatitis B infection in the National Infectious Disease Register (triangles: males; circles: females; all: crosses). The estimated true incidence of acute hepatitis B infection is shown by boxes with 95% Bayesian credible intervals.

4. Discussion

Based on national surveillance data, both the incidence of acute and the prevalence of chronic hepatitis B infection have remained at very low levels in Finland. The estimated incidence of acute infection, adjusted for asymptomatic infections, was 4.2-fold compared to the register-based data, corresponding to 1.67 new infections per 100,000 per year. Even after the adjustment, the cumulative lifetime risk of acquiring acute hepatitis B infection in Finland is very small (0.13%), only one quarter of the estimated 0.55% in England and Wales [17]. In Finland, the number needed to vaccinate to prevent 1 acute hepatitis B infection is then roughly 800 (1/0.0013). The estimated cumulative risk of acute infection by 40 years is 0.11%. After accounting for the chronic carriers immigrating to Finland, only 1.2% of chronic carriage was inferred to follow from transmission in Finland. This follows from the fact that hepatitis B infections in neonates and in children have been extremely rare. In addition, four out of five chronic carriers were registered among foreign-born individuals, a vast majority of which have immigrated to Finland while already infected. Based on the estimated incidence of acute infection, the cumulative lifetime risk of chronic infection is 0.01%, i.e. 1 case per 10,000 individuals. For preventing 1 chronic infection, roughly 10,000 infants thus need to be vaccinated in a universal immunisation programme.

The estimated cumulative risk of acute infection by 40 years of age (0.11%) is substantially lower than the prevalence of hepatitis B antibodies in the most recent seroprevalence study in Finland, carried out nearly 20 years ago using residual serum samples from patients of Finnish origin having routine operations [12,14]. In that study, 2.8% of patients had been exposed to the virus by 40 years of age [12]. The difference may be explained by the different epidemiological situation in the late 1990s when the incidence of acute infection was substantially higher than today (Fig. 1).

Acute hepatitis B infection is typically acquired by young adults via some type of risk behaviour. Among Finnish-born males, three

Table 2
Hepatitis B cases in NIDR 2004–2012 and numbers of estimated acute and chronic infections. The data for the 9 years is presented in part (a) of the table. In part (b), the estimated annual numbers of preventable infections are presented in brackets.

Age group	Acute hepatitis B cases (NIDR)	Estimated acute infections (true)	Estimated chronic infections (projected)	Chronic hepatitis B cases (NIDR)
(a) The total number of cases in NIDR during 2004–2012 and derived estimates of infections				
All				
Infant (<1 year)	1	14	13	8
Children (1–11 years)	3	32	9	81
Teenagers (12–17 years)	9	66	7	164
Young adults (18–39 years)	113	527	31	1468
Middle and old aged (⩾40 years)	65	160	6	656
Total	191	799	66	2377[a]
Finnish-born				
Infant (<1 year)	1	14	13	4
Children (1–11 years)	0	0	0	11
Teenagers (12–17 years)	4	29	3	4
Young adults (18–39 years)	65	297	17	124
Middle and old aged (⩾40 years)	55	134	5	259
Total[a]	125	474	38	402
Foreign-born				
Infant (<1 year)	0	0	0	3
Children (1–11 years)	3	32	9	63
Teenagers (12–17 years)	5	37	4	158
Young adults (18–39 years)	48	230	14	1322
Middle and old aged (⩾40 years)	10	26	1	392
Total[b]	66	325	28	1938
(b) Potentially preventable infections in total (per year) by universal infant vaccination				
Infant (<1 year)	0[c]	0	0	
Children (1–11 years)	0	0	0	
Teenagers (12–17 years)	4 (0.4)	29 (3.2)	3 (0.3)	
Young adults (18–39 years)	65 (7.2)	297 (33)	17 (1.9)	
Middle and old aged (⩾40 years)	55 (6.1)	134 (14.9)	5 (0.6)	
Total	124 (13.8)	460 (51.1)	25 (2.8)	

[a] Including 37 chronic cases which could not be categorised as foreign- or Finnish-born individuals.
[b] Including acute (N = 6) and chronic (N = 356) hepatitis B cases with foreign names but missing country of birth information.
[c] Infections among infants were excluded from the analysis since they should be prevented by the current targeted vaccination programme in Finland.

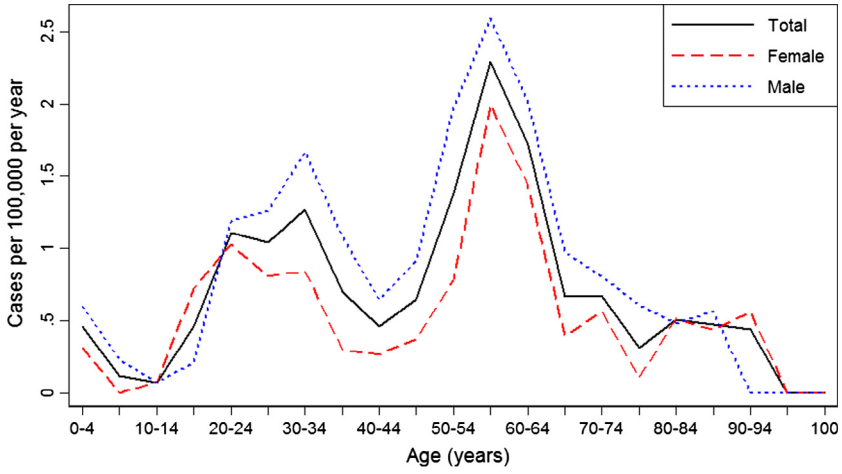

Fig. 3. Average annual notification rate of chronic hepatitis B in NIDR 2004–2012 among Finnish-born individuals.

quarters of the acute infections with information on the route of transmission were via sexual contact. Although injecting drug use has been an important risk factor in the past [19], it accounted for only 13% of the acute infections during 2004–2012. It is likely that targeted immunisations together with an extensive needle exchange programme have limited the role of injecting drug use in hepatitis B transmission in Finland. The needle exchange programme has limited the use of contaminated needles while providing an opportunity to vaccination at low-threshold services.

Due to the high proportion of hepatitis B transmission occurring via sexual contact, vaccinations among men who have sex with men (MSM) might be indicated. Finland has been the only northern European country not targeting MSM [10], although an increased risk in this group has been identified [20,21]. Nearly all pregnant

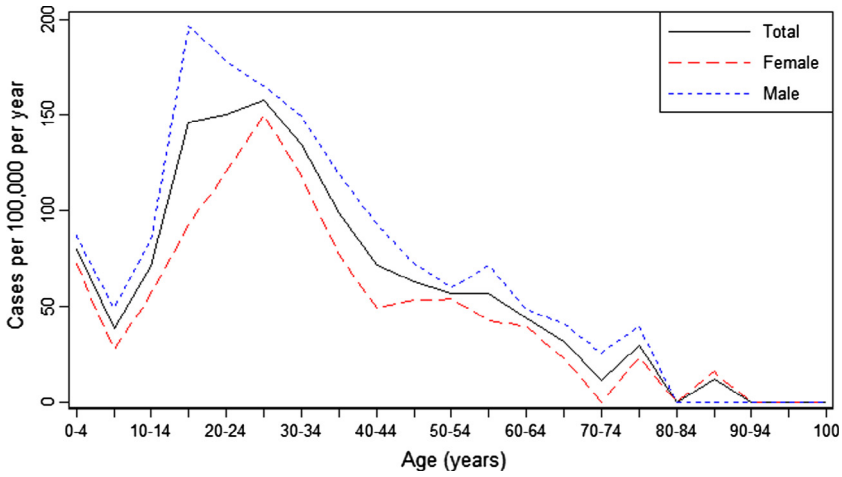

Fig. 4. Average annual notification rate of chronic hepatitis B in NIDR 2004–2012 among foreign-born individuals. All other than Finnish-born chronic cases were included in the calculations.

Table 3
Annual average migration of foreign-born individuals during 2004–2012 from regions with different HBV infection prevalence and the number of chronic carriers. Persons immigrating with chronic infection were calculated using age- and gender-specific WHO estimates of hepatitis B prevalence [6] by geographic region.

	To Finland Prevalence of HBV infection[a]				Net immigration Prevalence of HBV infection[a]			
	Low	Low inter-mediate	High inter-mediate[b]	High	Low	Low inter-mediate	High inter-mediate[b]	High
3 Main countries of birth	Sweden, Germany, USA	Russia or former Soviet Union, Estonia, Irak	China, Thailand, Somalia	Nigeria, Ghana, Cameroon	Sweden, Germany, UK	Russia or former Soviet Union, Estonia, Irak	China, Thailand, Somalia	Nigeria, Ghana, Cameroon
Age (years)	Persons (carriers, %)							
All	3772 (68, 1.8%)	10,966 (371, 3.4%)	3513 (212, 6.0%)	430 (41, 9.5%)	1878 (35, 1.9%)	9096 (312, 3.4%)	3030 (180, 5.9%)	383 (36, 9.4%)
Males								
<1	88 (2)	73 (3)	61 (4)	1 (0)	75 (2)	71 (3)	60 (4)	0
1–9	332 (8)	610 (28)	255 (13)	7 (1)	224 (6)	554 (25)	244 (12)	7 (1)
10–19	170 (4)	632 (26)	274 (15)	19 (2)	77 (2)	582 (24)	255 (14)	19 (2)
20–39	1312 (26)	3488 (120)	785 (54)	276 (27)	672 (13)	2838 (98)	639 (44)	251 (25)
⩾40	358 (6)	1022 (30)	159 (11)	15 (1)	102 (2)	707 (21)	89 (6)	4 (0)
Total	2260 (46, 2.1%)	5825 (206, 3.6%)	1534 (97, 6.2%)	318 (31, 10%)	1151 (24, 2.1%)	4752 (171, 3.6%)	1287 (80, 6.2%)	281 (28, 10%)
Females								
<1	83 (1)	61 (3)	65 (4)	1 (0)	72 (1)	58 (2)	63 (4)	0
1–9	313 (5)	563 (24)	259 (12)	9 (1)	219 (4)	517 (22)	249 (12)	9 (1)
10–19	161 (2)	546 (20)	299 (15)	11 (1)	65 (1)	489 (18)	284 (14)	11 (1)
20–39	818 (11)	2795 (87)	1148 (72)	86 (7)	353 (5)	2308 (72)	989 (61)	78 (7)
⩾40	136 (2)	1176 (31)	208 (13)	5 (0)	17 (0)	972 (25)	158 (10)	3 (0)
Total	1513 (22, 1.5%)	5141 (165, 3.2%)	1979 (115, 5.7%)	112 (10, 8.8%)	727 (11, 1.5%)	4344 (141, 3.2%)	1743 (100, 5.7%)	102 9 (8.8%)
Total	18,681 (691, 3.7%)				14,387 (563, 3.9%)			

[a] Map 2 for adults (19–49 years) [6] was used for country classification into HBV infection prevalence levels.
[b] Including 8% individuals with missing country of birth information.

women (98%) in Finland [22] take part in antenatal screening of hepatitis B. Because such organised screening is not carried out among men, the gender difference is likely to be even larger than what is routinely detected by surveillance. During 2004–2012, both acute (67%) and chronic (60%) infections were more common among men.

The proportion of foreign-born population has increased steadily in Finland during the last decades [23]. The increasing numbers of foreign-born individuals was not seen as increasing notification rates for hepatitis B cases during the study period (2004–2012). The majority of persons immigrating to Finland originate from countries with low-to-intermediate hepatitis B endemicity and several years' experience of universal immunisation programmes (Russia, Estonia). It can thus be expected that the number of carriers moving to Finland from these countries decreases rather than increases in the coming decades.

Electronic notification, received directly from laboratory software, is the foundation of data accuracy. In 2002, more than 70% of laboratory notifications were sent electronically to NIDR. In 2013, the corresponding proportion was already 96%. Because of the highly developed notification system, we estimated the incidence of acute infection assuming no underreporting. In fact, it is likely that we have overestimated the true incidence of acute infections since not all reported acute hepatitis B cases are symptomatic as now assumed. On the other hand, the limited number of acute cases among children elicits uncertainty to the assessment.

We estimated the number of acute and chronic hepatitis B infections preventable by an infant immunisation programme based on present force of infection. During the next decades, immunisation programmes elsewhere should diminish the number of carriers immigrating to Finland. As has been noted earlier, efforts outside a low-endemicity country will have a larger effect than interventions within [17,24]. A possibly changing epidemiology due to increasing immigration in the future is clearly an issue to account for when considering the possibility of a universal hepatitis B vaccination programme. Currently, however, there is no indication of a rising trend of hepatitis B transmission in Finland due to immigration alone. Nevertheless, it is of utmost importance that immigrating chronic carriers are recognised and treated and their next of kin vaccinated. In particular, young children should be vaccinated since they are at the highest risk of developing chronic infection. Based on the findings described in this paper, the targeted programme in Finland has recently been extended to include infants with either parent from a country with high to high intermediate HBV infection prevalence. This protects infants in families where screening is not carried out properly. Also MSM were included in the programme in 2016. To conclude, the functioning antenatal screening remains vital in preventing chronic hepatitis infection, which all in all is the major target of hepatitis B immunisation.

Contributors

TK contributed to acquisition, analysis and interpretation of data and drafting the article. KA contributed to statistical analysis and interpretation of data and drafting the article. MK contributed to interpretation of data and critically appraised the drafts. TL contributed to acquisition and interpretation of data and drafting the article. All authors contributed to the conception and design of the study and approved the final version of the manuscript to be submitted.

Funding

This study was funded by the National Institute for Health and Welfare, Finland.

Conflict of interest

None.

Acknowledgements

We thank Esa Ruokokoski, Jonas Sundman, Jan-Erik Löflund, Teemu Möttönen, Sari Jaakola and Maia Jeganova for their assistance in data collection and management. We also thank Markku Nurhonen and the hepatitis B vaccination working group members for their assistance in the investigation.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.vaccine.2016.11.090.

References

[1] Shepard CW, Simard EP, Finelli L, Fiore AE, Bell BP. Hepatitis B virus infection: epidemiology and vaccination. Epidemiol Rev 2006;28:112–25.
[2] Wright TL, Lau JYN. Clinical aspects of hepatitis B virus infection. Lancet 1993;342(8883):1340–4.
[3] Edmunds WJ, Medley GF, Nokes DJ, Hall AJ, Whittle HC. The influence of age on the development of the hepatitis B carrier state. Proc Biol Sci 1993;253 (1337):197–201.
[4] Hyams KC. Risks of chronicity following acute hepatitis B virus infection: a review. Clin Infect Dis 1995;20(4):992–1000.
[5] Centers for Disease Control and Prevention. Chapter 3 (Hepatitis B). In: CDC health information for international travel 2014. New York: Oxford University Press; 2014.
[6] Ott JJ, Stevens GA, Groeger J, Wiersma ST. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. Vaccine 2012;30(12):2212–9.
[7] Schweitzer A, Horn J, Mikolajczyk RT, Krause G, Ott JJ. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. Lancet 2015;386 (10003):1546–55.
[8] Beutels P. Economic evaluations of hepatitis B immunization: a global review of recent studies (1994–2000). Health Econ 2001;10(8):751–74.
[9] World Health Organization. Hepatitis B vaccines. Wkly Epidemiol Rec 2009;84 (40):405–20.
[10] Mereckiene J, Cotter S, Lopalco P, D'Ancona F, Levy-Bruhl D, Giambi C, et al. Hepatitis B immunisation programmes in European Union, Norway and Iceland: where we were in 2009? Vaccine 2010;28(28):4470–7.
[11] Van Damme P, Leuridan E, Hendrickx G, Vorsters A, Theeten H, Leino T, et al. Should Europe have a universal hepatitis B vaccination programme? BMJ 2013;10(347):f4057.
[12] Nardone A, Anastassopoulou CG, Theeten H, Kriz B, Davidkin I, Thierfelder W, et al. A comparison of hepatitis B seroepidemiology in ten European countries. Epidemiol Infect 2009;137(7):961–9.
[13] Varjonen V. Finland drug situation 2014. Helsinki, Finland: National Institute for Health and Welfare; 2015. Report No.: 3/2015.
[14] Leino T. Hepatiitti B -rokotusohjelman arviointi (Evaluation of hepatitis B vaccination programme). Helsinki, Finland: National Public Health Institute; 2006. Report No.: B9/2006.
[15] Basnet S, Onyeka IN, Tiihonen J, Fohr J, Kauhanen J. Characteristics of drug-abusing females with and without children seeking treatment in Helsinki, Finland. Scand J Public Health 2015;43(3):221–8.
[16] National Institute for Health and Welfare. Pakolaisten ja turvapaikanhakijoiden infektio-ongelmien ehkäisy (Prevention of infection problems among refugees and asylum seekers). Finland: Ministry of Social Affairs and Health; 2009. Report No.: 2009:21.
[17] Hahne S, Ramsay M, Balogun K, Edmunds WJ, Mortimer P. Incidence and routes of transmission of hepatitis B virus in England and Wales, 1995–2000: implications for immunisation policy. J Clin Virol 2004;29(4):211–20.
[18] Edmunds WJ, Medley GF, Nokes DJ. Vaccination against hepatitis B virus in highly endemic areas: waning vaccine-induced immunity and the need for booster doses. Trans R Soc Trop Med Hyg 1996;90(4):436–40.
[19] Hulkko T, Lyytikäinen O, Kuusi M, Seppälä S, Ruutu P. Infectious diseases in Finland 1995–2009. Helsinki, Finland: National Institute for Health and Welfare; 2010. Report No.: 28/2010.
[20] Valle SL. Sexually transmitted diseases and the use of condoms in a cohort of homosexual men followed since 1983 in Finland. Scand J Infect Dis 1988;20 (2):153–61.
[21] Ranki A, Valle SL, Antonen J, Suni J, Jokipii L, Jokipii AM, et al. Immunosuppression in homosexual men seronegative for HTLV-III. Cancer Res 1985;45(9 Suppl):4616s–8s.
[22] Surcel H, Haula T, Mäkelä M, Aho I, Hiltunen-Back E, Salo E, et al. Alkuraskauden infektioseulonta Suomessa (Screening of infectious diseases during early pregnancy in Finland). Helsinki, Finland: National Institute for Health and Welfare; 2014. Report No.: 7/2014.
[23] Organisation for Economic Co-operation and Development (OECD). International migration database. Foreign-born population (indicator); 2015. <https://data.oecd.org/migration/foreign-born-population.htm> [accessed 24.07.15].
[24] Marschall T, Kretzschmar M, Mangen MJ, Schalm S. High impact of migration on the prevalence of chronic hepatitis B in the Netherlands. Eur J Gastroenterol Hepatol 2008;20(12):1214–25.