INTERNATIONAL JOURNAL OF CIRCUMPOLAR HEALTH
2020, VOL. 79, 1817274
https://doi.org/10.1080/22423982.2020.1817274

Taylor & Francis
Taylor & Francis Group

ORIGINAL RESEARCH ARTICLE

Risk of hepatitis B when migrating from low to high endemic areas

Henrik Bygum Krarup[a,b], Karsten Fleischer Rex[c,d] and Stig Andersen[b,c,d,e]

[a]Department of Molecular Diagnostics, Aalborg University Hospital, Aalborg, Denmark; [b]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark; [c]Department of Internal Medicine, Queen Ingrid's Hospital, Nuuk, Greenland; [d]Arctic Health Research Centre, Aalborg University Hospital, Aalborg, Denmark; [e]Institute of Health, Ilisimatusarfik, Greenland University, Nuuk, Greenland

ABSTRACT

Prevalence of hepatitis B virus (HBV) infections varies markedly with geography and is endemic in the Arctic. Travel and migration have increased markedly while the influence of migration to high endemic areas remains unknown. We surveyed subjects migrating from an area with a low prevalence of chronic HBV infection (Denmark, 0.01%) to an endemic HBV area (West- and East Greenland, 3% and 29%) in order to describe the prevalence of HBV exposure among migrants. We included 198 Caucasian Danes that had migrated to Greenland and repeated the cross-sectional investigation after 10 years. We performed thorough serological testing for HBV. None had ongoing HBV infection. Migrants to East Greenland were more frequently exposed to HBV than those in West Greenland (34.3% vs 10.3%; $p < 0.01$). This difference was reduced at 10-year follow-up (8.1% vs 5.7%; ns) and the overall number of participants with past HBV infection decreased over the 10-year period from 19.4% to 6.9% ($p = 0.02$). In conclusion, migration from very low prevalence to endemic HBV areas associated with a markedly increased risk of exposure to HBV. Lack of vaccination among migrants from Denmark to Greenland was frequent and it poses a continuing risk. All who migrate from low to high endemic HBV areas should be vaccinated.

Abbreviations: HBV: Hepatitis B virus; HBV-DNA: Hepatitis B virus deoxyribonucleic acid; HBsAg: Hepatitis B surface antigen; Anti-HBs: Antibodies against hepatitis B surface antigen; Anti-HBc: Antibodies against hepatitis B core antigen; BMI: Body mass index

ARTICLE HISTORY
Received 26 June 2020
Revised 26 August 2020
Accepted 27 August 2020

KEYWORDS
Hepatitis B; migration; low endemic; high endemic; arctic; vaccination

Introduction

Infection with hepatitis B virus (HBV) is a global health burden with approximately 240 million people chronically infected [1,2] and estimated 600.000 fatalities each year from hepatocellular carcinoma or end-stage liver disease related to HBV [2].

HBV is transmitted through exposure to infected blood or bodily fluids. The risk of chronic infection is estimated to be below 5% in immune-competent adults exposed to HBV [3].

The prevalence of HBV infection differs with geography from low (prevalence <2%) in high-income countries to high (endemic, 8+ %) in low-income countries. The latter is characteristic of the Arctic countries and African countries south of Sahara while countries in Northern Europe are examples of the former [2,4].

Reports on the occurrence of HBV infection with migration are limited and they have focused on missionaries, healthcare and non-medical service workers [5–9] while data are lacking for the Arctic. Also, data on migration from, i.e. low prevalence Europe to endemic HBV areas, have been limited.

Greenland is an endemic area of HBV with regional differences. The prevalence of HBV exposure in the indigenous population in East Greenland was 88% of which 29% had chronic HBV infection. In parallel, 55% of the Inuit population in West Greenland had been exposed to HBV but only 3% had chronic HBV infection [10]. However, since 2010 vaccination has been implemented in Greenland in both newborns and 12-year-olds.

Greenland was a constituency in the Danish Kingdom until 2009, and travel and migration between Denmark and Greenland has been and still is considered as moving within the same country. Thus, the marked difference in the occurrence of HBV infection between Denmark and Greenland provides an opportunity to describe the prevalence of HBV exposure among migrants moving to an endemic area.

Methods

The present report concerns migrants from Denmark to Greenland and it is part of two cross-sectional population-based studies conducted in the same areas in Greenland in 1998 and 2008 [10,11].

CONTACT Henrik Bygum Krarup h.krarup@rn.dk Department of Molecular Diagnostics, Aalborg University, Aalborg DK-9000, Denmark

Subjects

Participants were 198 Caucasian men (80%) and women (20%) aged 50 to 69 years, and 31 participated twice. The places selected for investigation were Nuuk, the capital city in Greenland and Ammassalik district in East Greenland [10].

In Nuuk, a random sample of 25% of the total population of 1,920 [12] aged 50 to 69 years recorded to be living in the city was selected in 1998. In 2008, the same individuals were invited, and to add up to a similar number of participants in 2008 as in 1998, a random sample of the population was invited [11]. The total population of Nuuk aged 50 to 79 years was recorded to be 3,400 subjects in 2008. The total population aged 50 to 69 years in 1998 and 50 to 79 years in 2008 in Ammassalik district was recorded to be 358 and 541, respectively. All non-Inuit (Caucasian Danes) aged 50 to 69 years in Ammassalik district were included both in 1998 and in 2008. These participants were craftsmen and people working in the administration.

Data collection

Information on lifestyle pattern was obtained by interview-based questionnaires as described previously [10,11]. A venous blood sample was drawn with a minimal tourniquet, separated and stored at minus 20 degrees Celsius.

Laboratory tests

Blood samples were blinded using an 8-digit code and analysed in random order. All samples were tested for HBsAg. HBsAg negative samples were tested for anti-HBs and total antibodies against hepatitis B core antigen (anti-HBc(total)). Testing for HBsAg, anti-HBs, HBeAg, anti HBe and anti-HBc (total) was performed using HBsAg (V2), confirmatory HBsAg, AUSAB®, HBe 2.0, anti-HBe 2.0, CORE™ (Abbott Axsym™ System, Abbott Diagnostics AG, Wiesbaden, Germany). All serological testing was performed according to the manufacturer's instructions.

Individuals who were anti-HBs and anti-HBc positive were defined as naturally exposed to HBV while anti-HBV positive "only" were classified as vaccinees.

Statistics

Results are given as frequencies and Chi-squared test was used for comparison of frequencies between groups. Random selection of participants in Nuuk was performed using MedStat (Astra, Albertslund, Denmark). Data were processed and analysed using the Statistical Package for the Social Sciences version 13.0 (SPSS Inc., Chicago, IL, USA). A p-value of less than 0.05 was considered significant.

Ethical approval (505–99) by the Commission for Scientific Research in Greenland and written informed consent were obtained.

Results

The studies comprised a total of 1071 participants in 1998 and 2008, of which 873 were Inuit and 198 Caucasian Danes. The overall participation rate was 95% in 1998 and 80% in 2008. Among the Danes, 197 had migrated from Denmark to Greenland and the duration of residence above 10 years in Greenlandic is detailed in Table 1. The table also lists gender and age distributions as well as smoking and alcohol habits, and BMI. These did not differ between groups except for age and duration of residence between 1998 and 2008 participants. The differences in age and duration of residence were due to the recruitment procedure.

Table 2 lists the number of participants exposed to HBs antigen either by natural immunisation or vaccination. None had ongoing HBV infection and 75% had never been exposed to HBV in 1998 vs. 86% of new participants in 2008. The fraction of participants with past HBV infection decreased over the 10-year period from 19.4% to 6.9% ($p = 0.02$) among new participants. In East Greenland, the number of individuals with past infection decreased markedly (34.3% to 8.1%, $p < 0.01$). The number of vaccinated individuals was similar between 1998 and 2008.

One person participating twice seroconverted while 30 of the 31 persons who participated in both 1998 and 2008 had unchanged status.

The difference between participants in East Greenland and West Greenland is also shown in Table 2. Caucasians in East Greenland were more frequently exposed to HBV as compared to those living in West Greenland in 1998 (34.3% vs 10.3%; $p < 0.01$). This difference was reduced in 2008 (8.1% vs 5.7%; $p = 0.8$). The difference between East- and West Greenland in individuals never exposed to HBV had decreased from 20% in 1998 to 5% in 2008 ($p = 0.03$).

None of the 31 persons participating both in 1998 and in 2008 had moved between East and West Greenland. Six of the remaining had lived both places. The risk of infection did not change with the number of years living in Greenland (ns).

Even though the numbers are small it may be noticed that the number of vaccinated Caucasian Danes was similar between West- and East Greenland in 2008 (Table 2).

Table 1. Descriptives of 167 Caucasians migrated from Denmark to Greenland.

	1998		2008		1998 & 2008		2008 only	
	n	%	n	%	n	%	n	%
	94	100	104	100	31	100	73	100
Sex								
Men	75	79.8	83	79.8	29	93.5	54	74.0
Women	19	20.2	21	20.2	2	6.5	19	26.0
Age								
50–59 years	79	84.0	45	43.3	0	0.0	45	61.6
60–69 years	15	16.0	52	50.0	26	83.9	26	35.6
70–79	0	0.0	7	6.7	5	16.1	2	2.7
Participated in East Greenland †,‡	35	37.2	48	46.2	10	32.3	38	52.1
>10 years in East Greenland	25	26.6	26	25.0	10	32.3	16	21.9
>10 years in West Greenland	7	7.4	7	6.7	1	3.2	6	8.2
Participated in West Greenland ‡	59	62.7	56	53.8	21	67.7	35	47.9
>10 years in East Greenland	0	0.0	0	0.0	0	0.0	0	0.0
>10 years in West Greenland	47	50.0	46	44.2	21	67.7	25	34.2
Smoking								
Never	25	26.6	31	29.8	6	19.4	25	34.2
Past	17	18.1	31	29.8	12	38.7	19	26.0
Present	52	55.3	42	40.4	13	50.9	29	39.8
Alcohol §								
Never	9	9.8	19	18.4	5	15.2	14	20.0
< 14 units/week	65	70.6	66	64.1	18	54.5	48	68.6
> 14 units/week	18	19.6	18	17.5	10	30.3	8	11.4
BMI groups								
<18	1	1.1	1	1.0	0	0.0	1	1.4
18–25	35	37.6	27	26.5	8	26.7	19	26.4
25.1–30	40	43.0	50	49.0	18	60.0	32	44.4
>30	17	18.3	24	23.5	4	13.3	20	27.8

†Some participants in East Greenland had lived in West Greenland previously
‡Some participants had lived less than 10 years in Greenland
§Data missing in 3 participants

Table 2. The frequency of never and past HBV infection and HBV vaccination among Caucasians migrated from low endemic Denmark to high endemic Greenland.

		HBV infection		
		Never	Past	Vaccinated
		n (%)	n (%)	n (%)
1998 all		70 (75.3)	18 (19.4)	5 (5.3)
2008 all		86 (83.5)	11 (10.7)	6 (5.8)
1998 & 2008		24 (77.4)	6 (19.4)	1 (3.2)
2008 only		62 (86.1)	5 (6.9)	5 (6.9)
Living in	West Greenland			
	1998	48 (82.8)	6 (10.3)	4 (6.9)
	all 2008	49 (87.5)	4 (7.1)	3 (5.4)
	new 2008	31 (88.6)	2 (5.7)	2 (5.7)
	East Greenland			
	1998	22 (62.9)	12 (34.3)	1 (2.9)
	all 2008	37 (78.7)	7 (14.9)	3 (6.4)
	new 2008	31 (83.8)	3 (8.1)	3 (8.1)

Serum sample was missing in one participant in each of 1998 and 2008

Discussion

We identified two areas with a marked difference in the occurrence of HBV, shared citizenship and frequent migration with 25% of the population in Nuuk in West Greenland being Caucasian Danes. We investigated individuals who had moved from Denmark, an area with a very low HBV prevalence of 0.01% [13], to Greenland, an endemic HBV area [10]. Moreover, prevalence rates differed markedly between the two endemic HBV areas of East- and West Greenland. The investigation was repeated after 10 years in order to describe changes in the prevalence of HBV infection among migrants from Denmark to Greenland over time.

We found markedly higher HBV exposure in Caucasian Danes migrated to Greenland compared to reported prevalence in Denmark, and we found a difference in the occurrence of HBV exposure among Caucasian Danes between West- and East Greenland in 1998. The prevalence of HBV exposure had decreased markedly at 10-year follow-up, and the difference between endemic HBV areas was reduced.

Migration has been reported mainly from endemic areas to areas with a low prevalence of HBV. We investigated Greenlanders migrated to Denmark and found an HBV exposure of around 50% comparable to Greenlanders in West Greenland [14]. Harder et al. described a prevalence of HBV infection of 0.01% among women of Danish origin while it was 2.7% among foreign-born women in a surveillance programme of pregnant women in Denmark [13]. Similarly, Marschall and colleagues described a prevalence of HBV infection of 0.3% among women of Dutch origin while it was 3.8% among foreign-born women living in the Netherlands [15]. The occurrence

of acute HBV infection has declined even though the number of migrants has increased from 3% to 10% in the last two decades [16]. It seems thus that migration does not influence the prevalence of HBV among the native population in low prevalence countries.

Migrating from low prevalence areas to high endemic HBV areas associated with a seroconversion to anti-HBc among 5.5% of American missionaries working south of Sahara [7]. After 10-year service, 21.8% of missionaries in Africa contracted HBV infection [5]. Data on other groups than missionaries are scarce.

We investigated subjects with very low risk of work-related HBV exposure. Thus, the exposure was equal to that of the general population. At our first survey in 1998, the overall prevalence of HBV exposure was 20% with a geographical difference. It was 34% in East Greenland with a prevalence of HBV exposure in the indigenous population of 88% of which 29% had chronic HBV infection. In parallel, it was 10% in West Greenland where 55% of the Inuit population had been exposed to HBV but only 3% had chronic HBV infection. In our survey in 2008 the prevalence of a marker of HBV exposure was 8% and 6% among migrants in East and West Greenland, respectively, [10]. Thus, the overall number of exposed participants had decreased, and the geographical difference was evened out. The number of vaccinated participants was similar in 2008 and 1998, and the transmission was most likely based on sexual contact.

The Netherlands, UK, Norway and Sweden recently included HBV vaccination in their vaccination programmes, while it is not included in the national immunisation programme in Finland and Denmark. The Danish hepatitis prevention programme is targeted at high-risk groups, and the recommendation from the Danish National Board of Health specifies that health-care workers, working in Greenland, should be vaccinated against HBV [17,18]. Other groups are not included in the recommendation. We demonstrate that the increased risk includes all Danes working in Greenland. This emphasises that all migrants to Greenland should be vaccinated. We found less than 10% of migrants moving from Denmark to Greenland with positive anti-HBs-"only" suggestive of vaccination. This stresses the need for both awareness of the risk, and recommendation of vaccination prior to migration.

The number of study participants was limited but yet sufficient to provide insight into the influence of migration from very low prevalence to endemic HBV areas. The findings at 10-year follow-up demonstrate that the problem persists and calls for attention.

In conclusion, migration from very low prevalence to endemic HBV areas associated with a markedly increased risk of exposure to HBV. Lack of vaccination among migrants from Denmark to Greenland was frequent and it poses a continuing risk. All who migrate from low to high endemic HBV areas should be vaccinated.

Acknowledgments

We gratefully acknowledge the invaluable support from Queen Ingrid's Healthcare Center in Nuuk and staff at the hospital and nursing stations in East Greenland.

Disclosure statement

This study poses no conflicts of interest.

Funding

This study was supported by grants from: Greenland Government; Karen Elise Jensen Foundation; Northern Jutland Research Foundation.

Contribution by the individual authors:

HBK: Conception of idea, study design, raising of funds, analysis and interpretation of data, and writing of the manuscript.

KFR: Conception of idea, data collection, analysis and interpretation of data, and reviewing of the manuscript.

SA: Conception of idea, study design, raising of funds, data collection, analysis and interpretation of data, and writing of the manuscript.

References

[1] Schweitzer A, Horn J, Mikolajczyk R, et al. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. Lancet. 2015;386:1546–1555.

[2] Ott JJ, Stevens GA, Groeger J, et al. Global epidemiology of hepatitis B infection: new estimates of age-specific HBsAg seroprevalence and endemicity. Vaccine. 2012;30 (12):2212–2219.

[3] Sherloc S. The natural history of hepatitis B. Post Grad Med J. 1987;63:7–11.

[4] Rex K, Andersen S, Krarup HB. Hepatitis B among Inuit: a review with focus on Greenland Inuit. World J Hepatol. 2015;7(9):1265–1271.

[5] Lange RW, Frame JD. High incidence of viral hepatitis among American missionaries in Africa. Am J Trop Med Hyg. 1990;43(5):527–533.

[6] Steffen R. Risks of hepatitis B for travelers. Vaccine. 1990;8:S31–S32.

[7] Smalligan RD, Lange RW, Frame JD, et al. The risk of viral hepatitis A, B, C, and E among North American missionaries. Am J Trop Med Hyg. 1995;53(3):233–236.

[8] Stoney RJ, Jentes ES, Sotir MJ, et al.; the Global TravEpiNet Consortium. Pre-Travel preparation of US travelers going

abroad to provide humanitarian service, Global TravEpiNet 2009-2011. Am J Trop Med Hyg. 2014;90:533–559.
[9] Henriksen T-H, Lende S, Kaartinen L, et al. A og B (Hepatitis A and B). Tidsskr Nor Lægeforen. 1986;106(22):1686–1688.
[10] Krarup HB, Andersen S, Madsen PH, et al. Benign course of long-standing hepatitis B virus infection among Greenland Inuit? Scand J Gastroenterol. 2008;43(3):334–343.
[11] Andersen S, Rex KF, Noahsen P, et al. Forty-five year trends in overweight and obesity in an indigenous Arctic Inuit society in transition and spatiotemporal trends. Am J Hum Biol. 2014;26(4):511–517.
[12] Andersen S, Hvingel B, Kleinschmidt K, et al. Changes in iodine excretion in 50-60-y-old denizens of an Arctic society in transition and iodine excretion as a biomarker of the frequency of consumption of traditional Inuit foods. Am J Clin Nutr. 2005;81(3):656–663.
[13] Harder KM, Cowan S, Eriksen MB, et al. Universal screening for hepatitis B among pregnant women led to 96% vaccination coverage among newborns of HBsAg positive mothers in Denmark. Vaccine. 2011;29(50):9303–9307.
[14] Rex KF, Krarup HB, Laurberg P, et al. Population-based comparative epidemiological survey of hepatitis B, D, and C among Inuit migrated to Denmark and in high endemic Greenland. Scand J Gastroenterol. 2012;47(6):692–701.
[15] Marschall T, Kretzxchmar M, Mangen M-JJ SS. High impact of migration on the prevalence of chronic hepatitis B in the Netherlands. Eur J Gastrol Hepatol. 2008;20(12):1214–1225.
[16] Hansen N, Hay G, Cowan S, et al. Hepatitis B prevalence in Denmark – an estimate based on nationwide registers and a national screening programme, as on 31 December 2007. Euro Surveill. 2013;18(47):1–8.
[17] Sundhedsstyrelsen. Vejledning om forebyggelse mod viral hepatitis (Danish National Board of Health. Recommendations for prevention of viral hepatitis). Sundhedsstyrelsen; 2002.
[18] Sundhedsstyrelsen. Vejledning om HIV og hepatitis B og C virus. (Danish National Board of Health. Recommendations on HIV and hepatitis B and C virus). Sundhedsstyrelsen; 2013. [cired 2018 Jan 9]. https://www.sst.dk/~/media/AD9E0753B12546B8AEA323BF02AC3D2C.ashx