

# DISCHARGE DIAGNOSES OF LIVER DISEASES IN NUUK GREENLAND COMPARED TO A DANISH COUNTY HOSPITAL

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Received 15 February 2005; Accepted 8 February 2006

## ABSTRACT

**Background.** It is a frequently held notion that Inuits/Greenlanders are less prone to develop chronic liver disease than Europeans. High alcohol consumption and chronic viral infection are more frequent in Greenland than in Denmark.

**Study design.** A cross-sectional study to examine the incidence and prevalence of liver discharge diagnosis with focus on cirrhosis among hospital-admitted patients in Greenland and Denmark.

**Methods.** Register-based ICD-10 discharge diagnoses from Queen Ingrid's Hospital, Greenland, (n = 1072) and Randers Central Hospital, Denmark, (n = 4599) were used to compare the incidence and prevalence of cirrhosis in hospitalised patients during 1998.

**Results.** Five patients (0.47%) in Greenland and 36 (0.78%) in Denmark had a liver discharge diagnosis (OR = 0.67, 95% CI: 0.26-1.72). Two patients (0.19%) in Greenland compared to 25 (0.54%) in Denmark had a cirrhosis associated discharge liver diagnosis (OR = 0.34, 95% CI: 0.08-1.45). The number of newly diagnosed discharged patients was smaller in Greenland, 2 (0.19%), vs. Denmark, 14 (0.30%), (OR = 0.61, 95% CI: 0.14-2.70).

**Conclusion.** Discharge liver diagnoses were not more frequent in Greenland than in Denmark - if anything, the hospital prevalence and incidence of liver discharge diagnoses were lower. This may reflect fewer cirrhosis cases in Greenland, and/or a shorter survival time, or lack of follow up.

(*Int J Circumpolar Health* 2006;65(2):162-168.)

**Keywords:** liver cirrhosis, liver diseases, epidemiology, discharge diagnosis, hepatitis

## INTRODUCTION

The incidence of cirrhosis is increasing in most countries. The main causes are high alcohol consumption and chronic hepatitis B and C virus infection.

High alcohol intake (70-80 g/day) for at least 5 years seems to be necessary for the development of alcoholic cirrhosis (1;2). However, patients with alcoholic hepatitis, who continue to consume alcohol, will develop cirrhosis in up to 40% of the cases (3).

In Denmark, alcoholic liver cirrhosis has an incidence of 130 per million per year and a prevalence of 570 per million (4). For decades, the alcohol consumption in Greenland has been higher than in most other countries, including Denmark (5;6). Between 1987-2001, Greenlanders had an average intake per person approximately 20-25% higher than Danes, 14.5 L/person/year vs. 11.8 L/person/year (7).

At variance with Denmark, hepatitis B is considered endemic in the Greenlandic Inuit population (8;9), with an infectious rate of 40-75% and a HBsAg carrier status rate of 7-11% (9-11). The incidence of Hepatitis C (HCV) in Greenland is low and data on carrier status are sparse. In Denmark, the number of new cases of Hepatitis B per year is about 100, and the prevalence is 5,000-10,000 (0.1-0.2%). The incidence of HCV in Denmark is 15-20 per year and the prevalence is around 10,000-15,000 (0.2-0.3%).

Based on the higher alcohol consumption and the higher occurrence of especially chronic hepatitis B, we expected a higher occurrence of chronic liver diseases in the Greenland population than in the Danish population. The aim of the present study

was to test this assumption by comparing discharge diagnoses from comparable hospitals in the two countries, using the International Classification of Diseases (ICD-10). This aim should be considered in the light of the frequently held opposite notion that Greenlanders are less prone to develop cirrhosis with complications than are Danes and/or Europeans.

## MATERIAL AND METHODS

Study population: Eighty-five per cent of Greenland is covered by ice and the population of nearly 58,000 lives in scattered coastal urban centres, small towns and villages. Eighty percent of the population are living in one of the 16 urban centres affiliated to one of the district hospitals. The medical system is organised as in Denmark, and most physicians have been trained in Denmark. We obtained data from Queen Ingrid's Hospital, established in 1954 in Greenland's largest town, Nuuk. This hospital is the only one with a department of internal medicine, and patients from all of Greenland are directed to it.

In Denmark, data was collected from Randers Central Hospital, Department of Internal Medicine, which covers approximately 250,000 persons, with 62,000 living in the city of Randers. Randers is a medium sized typical Danish city, which is demographically representative of the Danish population (12).

Data on liver disease: Hospital discharge diagnoses were coded with reference to the 10th edition of the International Classification of Diseases. From both hospitals, we

identified all patients with a liver-related primary discharge diagnosis, K70.0-K77.0, B15.0-B19.0, and C15.0-C26.0, from 1<sup>st</sup> of January 1998 until 31<sup>st</sup> of December 1998. Patients were also identified by complications of liver disease i.e. ascites (R18.9), and variceal bleeding (I85.0-9). Clinical records of all cases were reviewed to establish the specific liver diagnosis. Data are given for all liver-related diagnoses in Table I, while diagnosis of cirrhosis and diagnosis associated with a later development of cirrhosis are given in Table II. At both hospitals, patients were registered with their unique personal identification numbers. Patients were characterised as incident cases if they had a first-time diagnosis in 1998.

In Greenland and Denmark, patients admitted to hospital with elevated liver enzymes or cirrhosis are screened for chronic viral hepatitis B and C in. Hepatitis B is screened by surface antigen (HBsAg), followed by further serologic testing for acute (IgM anti-core antibodies and/or HBV-DNA), or chronic (HBe antigen and/or HBV-DNA) infection, and hepatitis C is examined by anti-HCV antibodies and, if positive, HCV-RNA.

In Greenland, a total of 1590 discharged patients were registered, of which 259 were registered more than once and 259 patients were under the age of 18, leaving 1072 discharged patients. The review of the clinical records showed that only one of the five discharged patients with a liver diagnosis had a history of alcohol abuse. Two Greenland patients with "unspecific liver disease" were rediagnosed as one had alcoholic liver cirrhosis, and the other autoimmune hepatitis (Table I). We also checked that no patient was

transferred from other cities in Greenland directly to Denmark in 1998.

In Denmark, we started with 4642 discharged patients and excluded 43 patients under the age of 18, leaving 4599 discharged patients. Evaluation of the clinical records of the 36 patients with liver diagnosis showed that 18 patients had a history of alcohol abuse. Only 2 of the 17 patients with a diagnosis of cirrhosis did not have any history of alcohol abuse. None of the cirrhosis patients were, or had been, infected with hepatitis B or C. None of the two patients with hepatocellular carcinoma had cirrhosis or hepatitis.

## RESULTS

There were 1072 (42.0% male, 58.0% female) discharged patients in Greenland, and 4599 (51.1% male, 48.9% female) in Denmark ( $P < 0.001$ ), with a median age of 50 years (range 18-90) and 67 years (range 18-100), respectively ( $P < 0.01$ ).

In table I, all liver-related discharge cases and diagnoses are presented. A total of 5 persons in Greenland and 36 in Denmark were registered (OR = 0.67, 95% CI: 0.26-1.72). The total number of chronic hepatitis- and alcohol-associated liver diagnoses were lower in Greenland, with 2 (0.19%) patients compared to 25 (0.54%) in Denmark (OR = 0.34, 95% CI: 0.08-1.45) (Table II).

The clinical records showed both of the two discharged cirrhosis patients in Greenland to be incident cases, whereas in Denmark only 14 out of 36 cases were incident. Thus, the frequency of incident cases of cirrhosis was also smaller in Greenland than in Denmark (OR = 0.61, 95% CI: 0.14-2.70) (Table II).

**Table I.** Number of patients with a liver-related ICD-10 discharge diagnosis in 1998 from Denmark and Greenland.

Discharge diagnosis code	Denmark (n = 4599)	Greenland (n = 1072)
K70.1- Alcoholic hepatitis	3	0
K70.3- Alcoholic liver cirrhosis	10	1
K70.9- Alcoholic liver disease without specification	1	0
K71.2- Toxic liver disease with acute hepatitis	1	0
K73.2,9- Chronic active hepatitis without specification	7	1
K74.6- Liver cirrhosis without specification	7	0
K75.0- Liver abces	1	0
K75.2- Reactive hepatitis without specification	0	1
K76.9- Liver disease without specification	2	0
C22.0,7,9- Hepatocellular carcinoma	2	1
B16.9- Hepatitis B acuta viralis without specification	1	1
B18.1- Hepatitis B viralis chronica without delta agent	1	0
Total	36/0.78%	5/0.47%
OR (95% CI)	0.67 (0.26-1.72)	

**Table II.** Incident and prevalent number of hospitalised patients with a discharge diagnosis of cirrhosis and diagnoses associated with later development of cirrhosis.

Diagnosis code	Prevalent		Incident	
	Denmark (n = 4599)	Greenland (n = 1072)	Denmark (n = 4599)	Greenland (n = 1072)
K70.1- Alcoholic hepatitis	3	0	1	0
K70.3- Alcoholic liver cirrhosis	7	1	4	1
K70.9- Alcoholic liver disease without specification	1	0	1	0
K73.2- Chronic hepatitis without specification	5	1	3	1
K74.6- Liver cirrhosis without specification	6	0	3	0
K76.9- Liver disease without specification	2	0	2	0
B18.1- Chronic viral Hepatitis B	1	0	0	0
Total	25/0.54%	2/0.19%	14/0.30%	2/0.19%
OR (95% CI)	0.34 (0.08-1.45)		0.61 (0.14-2.70)	

The confidence intervals of the frequencies are wide, and differences are not statistically significant.

## DISCUSSION

We found that the frequency of patients discharged from hospital with a diagnosis of liver disease, including both incident and

prevalent cases, was lower in Greenland than in Denmark; however, confidence intervals were wide. This seems to refute the assumption of higher occurrence of liver disease in Greenland, as based on the more frequent occurrence of risk factors.

Conversely, the lower number of prevalent and incident cases in Greenland may be in accordance with, and could partly explain, the clinical notion that liver disease is more

rare among Greenlanders. This is the first study from Greenland using hospital ICD-10 discharge diagnoses to examine the total and newly diagnosed number of hospitalised patients with liver diseases. This was possible because all discharges were manually recorded and made electronically accessible for one year by one of the authors (HSP). The validity of the ICD hospital discharge diagnosis of cirrhosis in Denmark has previously been reported to be high, i.e. 85% (13). However, variation in the predictive value between specialized and non-specialized departments has been reported for other diseases, like stroke and inflammatory bowel disease (14-16). Therefore, we reviewed the clinical records of registered liver patients in Denmark and Greenland, to make sure that patients were correctly diagnosed. Two of the patients from Greenland had a revision of their liver diagnosis and all patients from Denmark were correctly diagnosed. We also precluded the transfer of patients with liver diseases directly to Denmark from the local Greenland hospitals.

The primary limitation of this study is the small number of patients. Unfortunately, only data from 1998 were available for Greenland. Furthermore, because of the large distances between Greenland health centers and the hospital, there may be a report bias favouring low numbers of liver patients being registered in Greenland. On the other hand, it is the impression from clinical work on location (H.S.P.), that nearly all patients with liver diseases in Greenland are seen at Queen Ingrid's Hospital in Nuuk. This may balance the former bias.

Only the first discharge diagnosis listed was available from Greenland and, therefore,

we used similar data from Denmark. This may have led us to underestimate the number of patients with discharge diagnoses of liver diseases at both places.

Our findings contrast with the higher incidence of chronic viral hepatitis and higher alcohol consumption in Greenland than in Denmark. The risk of developing cirrhosis increases with age and our finding of a possible lower occurrence of cirrhosis may be confounded by the fact that the Greenlanders' average age was ten years lower than that of the Danes. However, an earlier combined autopsy and mortality registry study also indicated a lower occurrence of cirrhosis (and of hepatocellular carcinoma) in Greenland (17). However, there seems to be a small increase in liver cancers during the past decades (18;19). In an elaborate health survey performed during the period 1999-2001 in Greenland, the prevalence of markers of cirrhosis i.e. icterus, spider naevi, or ascites, were observed in 0.1-0.5% of the subjects studied (6), which may suggest a higher occurrence of liver disease than would be expected from our data.

The high HBsAg carrier frequency (7-11%) has been observed following serological testing of asymptomatic Greenlanders in epidemiological studies (9-11). This, together with our data, may thus suggest that either HBV infection is less clinically manifest, or that the patients with acute and/or chronic HBV infection are less frequently admitted to the hospital.

Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) with subsequent development of cirrhosis are only sparsely described in Greenland and Denmark. None of the patients from Green-

land were diagnosed with NAFLD/NASH. However, raised liver enzymes have been found in 2-3% of Greenlanders (6). Furthermore, obesity is increasing in Greenland and body mass index (BMI) data indicates that approximately 34% of men and women are overweight (BMI = 25-29.9) and 19% obese (BMI > 30) (6). Thus, NAFLD/NASH may be an under-recognized condition in Greenland and awaits further investigations.

In the Greenland discharge data, it is not possible to distinguish between Inuit and Danes (13% of the population). However, the patient records in both countries showed that all patients with liver diseases had the ethnicity of the country in which they were registered. Furthermore, diagnosis distribution in Randers was compared with the National Danish Patient Registration. The Randers data were representative for Denmark, also regarding liver diagnoses (the national incidence of liver diseases is 0.069%, compared to 0.057% observed in Randers).

Data of discharge diagnoses in Greenland are not administratively accessible, as electronic registers have not yet been established. However, such registers will apparently be implemented in the near future, hopefully for both administrative and research purposes.

With reservation for the small number of patients available for analysis, it appears that the higher occurrence of the risk factors, viral hepatitis and high alcohol intake, does not lead to a higher incidence of chronic liver disease in Greenland. Thus, it remains possible that genetic, or environmental factors may protect Greenlanders from the development of chronic liver disease. This warrants further studies based on larger data materials that, hopefully, will be available in the future.

## Acknowledgements

Rigshospitalet, Copenhagen and Medical Department, Randers Central Hospital, Denmark are thanked for assistance regarding patient records.

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