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Living conditions, quality of life, adherence and treatment outcome in Greenlandic HIV patients

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Objectives. Despite a high level of sexually transmitted infections, HIV incidence has remained quite stable in Greenland with 5–6 new cases per year (approximately 10 per 100,000). However, disease control is suboptimal and mortality is relatively high. The aim of the present study was to determine associations between adherence to treatment and treatment outcome, living conditions and quality of life among HIV patients in Greenland.

Material and methods. Cross-sectional questionnaire-based cohort study of HIV patients in Greenland during 2008–2009. Data regarding treatment, viral load, CD4 count, etc. were obtained from a central HIV-database.

Results. Forty-six persons, 17 women and 29 men, of the 60 registered HIV-positive patients (77%) were included. Eighty percent were heterosexually infected and 17% by men having sex with men (MSM) activity. Median age at the time of diagnosis was 48 years (range 20–63). Eighty-nine percent received highly active antiretroviral therapy (HAART). Sixty-seven percent were adherent as defined by a combination of adherence to appointments and to treatment. Ninety-seven percent of adherent and 17% non-adherent patients on HAART had HIV-RNA less than 200 copies per ml (RR = 24.2, $p < 0.0001$). Poor adherence was associated with younger age (< 50 years) (adjusted RR = 7.95, $p = 0.005$) and living in remote areas with no direct contact with skilled personnel (adjusted RR = 6.75, $p = 0.01$). Unsafe sex was also more frequent among non-adherent patients (RR = 4.12, $p = 0.026$), but due to few answers this topic was not included in the multivariate model.

Conclusion. The HIV population in Greenland is peculiar since most patients are heterosexually infected and middle-aged at diagnosis. A relatively poor adherence and consequently inferior treatment outcome is related to young age and living in remote areas.

Keywords: *HIV*; *Greenland*; *adherence*; *living conditions*; *quality of life*

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Greenland is a huge country of 2,166,086 km^2 with a population comprising about 56,000 inhabitants (1). About 16,000 live in the capital, Nuuk, and the rest in 15 small towns and a number of settlements scattered along the coastline (1). Life expectancy is 66 years for men and 71 years for women (1). Main occupation is fishing (1). About 40% of the population over 15 years of age receive public help such as old age pension or disability pension (1). Average income for persons above 14 years of age is 35,000 USD per year (1). A central hospital, Queen Ingrid's Hospital, is located in Nuuk, while smaller district hospitals are located in each of the 15 towns. The first HIV case in Greenland was observed in the mid-1980s (2). Because of the high incidence of sexually transmitted infections (3) an explosive HIV epidemic was feared. However, the epidemic has remained quite stable with about 5 new cases per year (4). We have previously shown that most patients are infected through heterosexual contact and are middle-aged at the time of diagnosis (5). In a molecular epidemiological study we found that HIV was introduced at least 9 times into Greenland, and that one of these introductions had given rise to a circulating epidemic, including 76% of all infected persons (6). Many patients belong to socially marginalized groups burdened by low income, unemployment

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and heavy drinking, forming 2 distinct subgroups located in the 2 largest towns, Nuuk and Sisimiut (5). Even though highly active antiretroviral therapy (HAART) is free of charge in Greenland, we have found that treatment outcome is relatively poor and overall mortality relatively high, around 11% per year for patients on HAART during 1997–2003 (5). Although improving, treatment outcome still remains inferior to Denmark (7). A 25% prevalence of transmitted drug resistance corresponds well with the impression of low drug adherence and high-risk behaviour (8).

The reasons for the disappointing outcome and treatment results in Greenland are unknown, but may include the vast geography in Greenland with often long distances to health care facilities, lack of specialized physicians, difficulties in having sufficient laboratory control, and patient-related factors such as comorbidity and poor compliance.

Optimal adherence to treatment is known to be essential for maximal suppression of viral replication and for avoidance of drug resistance (9,10) and it is a critical determinant of survival in HIV patients (11–13). Elsewhere in the world a number of social, clinical and economic factors have been found to influence compliance (14,15) and quality of life of HIV patients (16), while there is no information of such factors in the Greenlandic HIV population. The aim of this study was to describe the association between adherence to treatment and treatment outcome as well as the associations between adherence and living conditions and quality of life, respectively, among HIV-positive persons in Greenland.

Material and methods

The study was conducted in 2008–2009. During these years there were 60 registered HIV-positive patients in Greenland, most of whom lived in the 2 towns of Nuuk and Sisimiut (Fig. 1).

HIV patients living in Nuuk are treated at the central Queen Ingrid's Hospital in Nuuk, while in the districts HIV treatment and control are guided from Queen Ingrid's Hospital, but administered by unspecialized local health personnel. All supervision of HIV patients and initiation of HAART are performed by one of the authors (KL). Patients living in Nuuk are controlled in the outpatient clinic every 3–4 months, and in the districts at least twice a year, the latter mainly due to logistic reasons with sample shipping. Blood samples for HIV-RNA and CD4 cell counts are sent by courier to Denmark. Plasma samples are analysed for HIV-RNA at the Department of Virology, Statens Serum Institut, Copenhagen, and CD4 cell count at Rigshospitalet, Copenhagen. In Greenland, treatment with HAART is implemented when CD4 count is below 350 cells per µl. Plasma is assayed for genotypic resistance in all

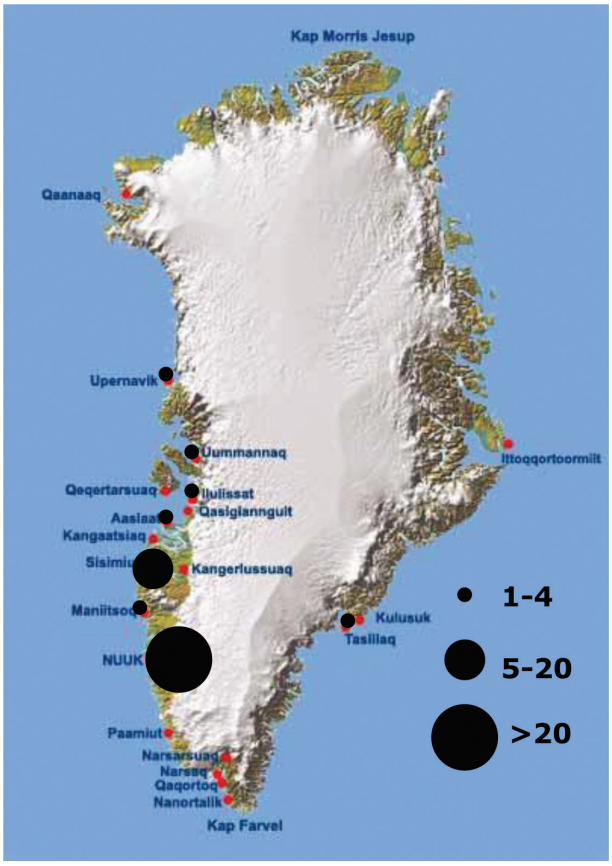

Fig. 1. Geographical distribution of HIV patients in Greenland.

patients at the time of HIV diagnosis and in case of HIV-RNA >1000 copies per ml. Treatment is adjusted in accordance with the resistance pattern. All HIV patients in Greenland including data on viral load, CD4 counts, etc. are registered in a central database www.infcarehiv.dk.

In this study we used available data from the central HIV database mentioned above. Virologic failure was defined by 2 repeated HIV RNA >200 copies per ml (17). To collect data on living conditions and quality of life, all known HIV-positive patients were asked to fill in a questionnaire during a routine outpatient visit in the study period 2008–2009. Most patients were interviewed or guided by a Greenlandic speaking doctor (MR) not responsible for the clinical care of the patients. The questionnaire was a modification of a questionnaire used for a study of 1,212 HIV-positive Danes (18) and comprised questions regarding living conditions and life quality issues. The modification included questions about Inuit ethnicity and specific Greenlandic socio-demographic issues. "Inuit" was defined by both parents being born in Greenland, "mixed" when one of the parents was born in Greenland and one elsewhere or "of unknown origin", and as "non-Inuit" if none of the parents were known to be born in Greenland.

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Adherence was defined as being seen in the outpatient clinic at least twice a year, and when on HAART having taken the last dose of medicine within 24 hours and not having skipped a dose within the last 4 days. If not fulfilling these criteria the patients were defined as non-adherent.

Statistics

The relative risk of HIV progression measured by high viral load and low CD4 count for non-adherence versus adherence was calculated as the proportion of non-adherent patients with such markers divided by the proportion of adherent patients using a binomial log-linear regression model in proc Genmod in SAS v9.2. The relative risks of non-adherence according to a wide range of living conditions and quality of life markers were calculated in a similar way. When having cells with 0 observations, no RR was estimated and the differences in proportions were evaluated by an exact Pearson Chi-square test in Proc Freq in SAS. From these univariate analyses a multivariate analysis was carried out by including significant variables ($p < 0.05$) in a single model and then using backward elimination until all remaining factors had reached significance.

Ethics

The investigation was scientifically and ethically approved by The Commission for Scientific Research in Greenland. Written informed consent was obtained from all participants. The study fulfilled the Helsinki II Declaration. Patients were informed that their responses remained confidential and would have no consequences for their treatment.

Results

Forty-six (77%) patients participated in the study, 17 women and 29 men aged 23–74 years with a median of 56 years. Virus transmission route was by heterosexual activity in 37 patients (80%) and by men having sex with men (MSM) activity in 8 (17%). One patient was a former drug addict and probably infected through i.v. drug abuse. Four of the five patients younger than 40 years were homosexual men. The patients had their HIV diagnosis established between 1 and 18 years, median 7 years, prior to the interview. Age at HIV diagnosis ranged from 20 to 63 years, median 48 years. Thirty-seven patients were infected in Greenland, the remaining 9 abroad, mostly in Denmark. Forty-four of the patients were born in Greenland. By the definition used, 43 were Inuit, 1 non-Inuit and 2 of mixed origin. Forty-one of the patients received treatment with HAART, and 5 were untreated. Twenty-five of the participating patients lived in Nuuk, and 21 in the districts (Fig. 1).

Of the non-participating 14 patients, 3 women and 11 men (median age at diagnosis 55 years, range 31–64 years), 3 refused to participate, 3 lived in remote areas, 1 was in jail and 2 failed to attend appointments. Furthermore 5 registered HIV-positive patients had refused treatment and control in the clinic. These 14 patients had been tested HIV-positive between 2 and 13 years (median 7 years) prior to the study. Thirteen of them were heterosexually infected and 1 by MSM activity.

Thirty-one patients (67%) were found to be adherent according to definition. Twenty-nine (71%) of those treated with HAART stated that they had taken at least 90% of the prescribed drugs within the last 30 days and none of them had missed a dose within the last 4 days.

There was a significantly higher rate of sufficient virologic response among adherent patients on HAART than among non-adherent on HAART, and more adherent patients had CD4 cell counts exceeding 350 cells per µl (Table I). Although overall only 73% had sufficient virologic suppression, almost all (97%) adherent patients had viral loads <200 copies per ml in contrast to only 17% of non-adherent.

Table II shows socio-demographic features among adherent and non-adherent patients. There was a significant difference in age distribution ($p = 0.003$) with adherent patients being relatively older (median 58 years, range 45–74) than non-adherent patients (median 49 years, range 23–60) (Fig. 2), and more of them receiving an age-related pension. Adherence was significantly better among patients living in Nuuk than among patients living in the districts outside of Nuuk. Fifty percent of those infected through MSM activity were

Table I. Association between adherence and virologic response to HAART and CD4 count among 46 HIV patients from Greenland 2008 to 2009

	HIV-RNA in patients on HAART*				CD4 count			
	<200 copies/ml	≥200 copies/ml	RR	p-Value	≥350 cells/µl	<350 cells/µl	RR	p-Value
Adherence (n = 31)	28	1	1 (ref.)		26	5	1 (ref.)	
Non-adherence (n = 15)	2	10	24.2 (5.60, 420)	<0.0001	5	10	4.13 (1.84, 11.4)	0.001

*41 patients on HAART.

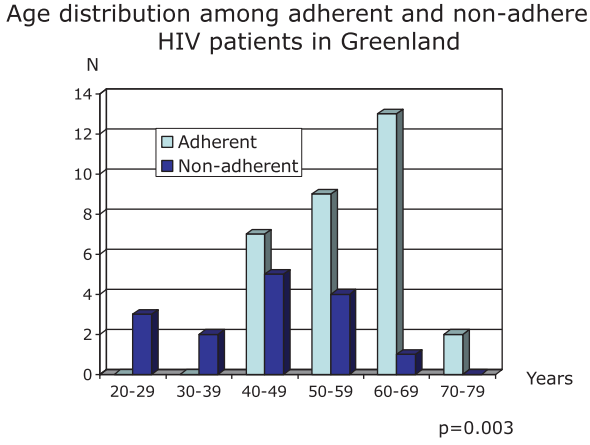

Fig. 2. Age distribution among adherent and non-adherent HIV patients in Greenland.

non-adherent compared with 27% of heterosexually infected, but the numbers are small and the difference is not significant (Table II). There was no difference with regard to duration of HIV or of treatment with HAART or having an AIDS-defining event, and no difference with regard to education or financial situation. Fifty-seven percent of the patients had only basic school education. Regarding quality of life (Table III) there was no difference between the 2 groups as to self-perception of health, having a steady partner, or living alone and no difference with regard to having friends or feeling lonely. Overall, 85% of patients considered their health to be good or fair. Eighty percent lived alone (data not shown). One of the patients was homeless. There was no difference between the 2 groups with regard to sexual activity or satisfaction, but unsafe sex was significantly more common among non-adherent patients (Table III). Sexual activity was inversely related to age (data not shown). Alcohol and tobacco use did not differ significantly among the 2 groups although both showed a trend for association to non-adherence. It is remarkable that 13 (28%) of the patients abused hash, 3 of them daily (Table III).

By multivariate analysis, young age and living in a district as opposed to Nuuk were found to be the 2 factors independently associated with poor adherence (Table II). Due to few answers unsafe sex was not included in the multivariate model.

Discussion

This study is, to our knowledge, the first study among HIV patients in an Arctic population of living conditions and quality of life and their association with adherence and treatment outcome. The HIV population in Greenland differs from most other HIV populations throughout the world, as most patients are relatively old at the time of diagnosis, reflecting late infection rather than late diagnosis (5), and as most are infected heterosexually. Most HIV patients in Greenland are uneducated and live alone. As the main part are unemployed they are relatively poor with 76% in our study reporting an income less than 20,000 USD per year compared with 64% of the Greenland population as a whole (1).

There are no universally accepted criteria of adherence in HIV patients, and different criteria have been used (13,19–21). We used a combination of adherence to appointments and to medication, as both are crucial for optimal infection control. According to these criteria 33% of the patients were non-adherent. Although the results are not directly comparable with other studies (10,13,22), the fraction of non-adherent HIV patients in Greenland seemed relatively high especially when considering that 8% of the registered HIV population had refused to participate in the HIV treatment program and had skipped appointments for years.

One patient who asserted to be adherent had a viral load of more than 80,000 copies per ml despite full viral sensitivity to his treatment, which questions the validity of his statement. Even so there was such a strong association between adherence and disease control with adherent persons having substantially lower viral loads and higher CD4 counts than non-adherent patients that it, like elsewhere in the world, underlines the importance of adherence.

We found that only 2 factors were independently associated with adherence, old age and living in the capital Nuuk. Studies from other parts of the world have indicated that the health care provider's level of knowledge, experience and skills are of great importance for patient adherence, as is the level of support and encouragement (14). In agreement with those results we found that living in a district outside of Nuuk was associated with poor adherence. While the staff situation may differ between the district hospitals, in general patients from the districts have no direct contact with HIV-committed personnel. This emphasizes the importance of having dedicated and skilled health staff members to take care of this patient group.

The finding that adherence was highest among elderly people on age pension is supported by results from other studies showing that adherence improves with age of the patient (19,21). Related to the relatively high age, a large fraction of the patients were sexually inactive and many of them had no sexual needs, but sexual activity was relatively high among the young patients with poor adherence. Fifteen percent of the patients reported having had unsafe sex within the last year. The fraction might be higher since many patients refused to answer this question. It warrants attention that unsafe sex was significantly associated with non-adherence.

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Table II. Association between adherence and socio-demographic and clinical data among 46 HIV patients from Greenland 2008 to 2009

	Adherent (n = 31)	Non-adherent (n = 15)	RR non-adherence	p-Value	Adjusted RR*	p-Value adjusted
Sex				0.35		
Males	21	8	1 (ref.)			
Females	10	7	1.49 (0.63, 3.48)			
Age				0.004		0.005
> 50 years	24	5	1 (ref.)		1 (ref.)	
< 50 years	7	10	3.41 (1.49, 9.51)		7.95 (1.85, 43.6)	
Place of living				0.01		0.01
Nuuk	21	4	1 (ref.)		1 (ref.)	
Districts	10	11	3.27 (1.34, 10.5)		6.75 (1.56, 38.4)	
Route of infection				0.22		
Heterosexually	27	10	1 (ref.)			
MSM	4	4	1.85 (0.64, 4.18)			
AIDS defining events				0.84		
No	24	12	1 (ref.)			
Yes	7	3	0.9 (0.24, 2.23)			
Duration of HAART**				0.19		
0–4	8	6				
5–9	16	6				
> 9 years	5	0				
Special education/ skilled training				0.74		
Yes	12	7	1 (ref.)			
No	17	8	0.87 (0.37, 2.08)			
Occupation				0.02***		
Full time	6	2	1 (ref.)			
Part time	1	5[a]	3.33 (1.16, 18.3)			
Pension	24	8	1.0 (0.32, 5.77)			
Financial support***				0.0007***		
Cash assistance	0	2				
Age pension	14	0				
Disability pension	10	9[a]				
Income USD per year				0.17		
< 10,000	1	2	1 (ref.)			
10,000–20,000	18	8	0.46 (0.19, 2.05)			
> 20,000	8	1	0.17 (0.01, 1.14),			
Financial situation				0.81		
Good	9	4	1 (ref.)			
Fair	10	4	0.93 (0.27, 3.23)			
Poor	11	7	1.26 (0.48, 4.02)			

Note: There may be missing values when the patients refused to answer the question.
*Adjusted for other significant factors.
**Due to convergence problems /empty cells, no RRs are presented and the p-values presented are from an exact Pearson χ^2 test.
***Due to correlation between the variables "Occupation" and "Financial support", "Occupation" was chosen to be included in the multivariate analysis because "Financial support" is a subset and thus excludes otherwise valid observations.
[a]One patient working part time also received disability pension.

Table III. Association between adherence and life style and quality of life indicators among 46 HIV patients from Greenland 2008 to 2009

	Adherent (n = 31)	Non-adherent (n = 15)	RR non-adherence	p-Value	Adjusted RR*	p-Value adjusted
Self-perceived health				0.83		
Good	20	9	1 (ref.)			
Fair	7	3	0.97 (0.25, 2.57)			
Poor	4	3	1.38 (0.38, 3.43)			
Steady partner				0.96		
Yes	6	3	1 (ref.)			
No	25	12	0.97 (0.40, 3.61)			
Do you have friends?				0.23		
Yes	25	14	1 (ref.)			
No	6	1	0.4 (0.02, 1.54)			
Does it happen that you are alone even if you want to be with others?				0.26		
Often	7	1	1 (ref.)			
Now and then	9	7	3.5 (0.80, 59.8)			
Seldom/never	12	5	2.35 (0.47, 41.2)			
Sexual activity				0.11		
At least once a month	10	8	1 (ref.)			
Less than once a month	4	3	0.96 (0.27, 2.38)			
Not within the last year	13	2	0.3 (0.05, 0.98)			
Unsafe sex*				0.026		0.063
Not within the last year	18	4	1 (ref.)		1 (ref.)	
At least once within the last year	1	3	4.12 (1.24, 13.4)		14.3 (0.87, 654)	
Satisfaction of sexual needs				0.66		
Yes	10	4	1 (ref.)			
No	6	3	1.17 (0.28, 4.22)			
No sexual needs	6	1	0.5 (0.03, 2.68)			
Alcohol use				0.07		
Never-once per month	17	3	1 (ref.)			
2–4 timers per month	11	9	3.0 (1.07, 12.1)			
At least 2 times per week	3	3	3.33 (0.80, 14.5)			
Tobacco smoker				0.06		
No	9	1	1 (ref.)			
Yes	21	14	4.0 (0.98, 68.1)			
Hash abuse				0.23		
No	24	9	1 (ref.)			
Yes	7	6	1.69 (0.69, 3.81)			

Note: There may be missing values when the patients refused to answer the question.
*Due to few answers not included in the multivariate model, but adjusted for age and place of living.

Although not significant, we found a trend towards higher adherence with higher income. In accordance with this it has been shown that low educational levels are associated with poorer HIV outcome (20). Many HIV patients in Greenland are uneducated and relatively poor. Although treatment is free of charge the finding may indicate that financial situation influences compliance.

In contrast to others we found no association with HIV history such as duration of HIV or of HAART treatment or having an AIDS-defining event (11). Others have found that support from family improves compliance (14,22). Most patients in the present study lived alone without a steady partner, and although most of them reported to have friends and only few felt lonely, it

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is possible that a higher degree of support from relatives could be helpful.

Alcohol abuse has previously been reported to be common among HIV patients in Greenland (5). The present study did not confirm that since only 13% of the patients had a weekly alcohol intake while, although not legalized, hash abuse was relatively common. However, there was an insignificant trend of use of alcohol being associated with poor adherence.

It should, however, be considered that some of the characteristics associated with poor adherence, e.g. low income and alcohol abuse, could actually be results of low compliance and thus progression in HIV disease rather than the opposite. This study is cross-sectional and does not reveal causal associations. To determine such causal relationships longitudinal studies with knowledge of pre-infectious status are needed.

Poor drug-adherence is associated with increased morbidity and mortality (11–13) and the low compliance among relatively young patients warrants a special effort for this group. Directly observed therapy (DOT) has been promoted by the WHO to improve adherence to tuberculosis programs and has also been suggested for HIV treatment. However, systematic reviews of randomized trials showed no benefit of this strategy, neither towards tuberculosis (23) nor towards HIV (24).

It is possible that earlier initiation of HAART with newer simplified drug regimens can improve adherence in vulnerable patient groups (25). In Greenland especially young homosexual men with a high level of sexual activity could be a target for such strategy, and we would thereby not only improve treatment outcome, but also reduce HIV transmission (26).

Conclusion

Poor adherence and consequently inferior treatment outcome are common among Greenlandic HIV patients, especially in the younger age groups and among patients living in areas outside of the capital Nuuk. The results indicate that close attention should be paid to these groups of HIV patients to improve adherence and reduce HIV-related morbidity and mortality.

Conflict of interest and funding

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