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Thalassemia and sickle cell anemia in Swedish immigrants: Genetic diseases have become global

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Abstract

Aims: Some 15% of the Swedish population is born outside Sweden, originating from all continents of the world. Thalassemia and sickle cell anemia constitute the most common inherited recessive disorders globally and they are endemic in areas of Africa and Asia, origins of many immigrants to Sweden. We aimed at investigating the origins of the Swedish sickle cell and thalassemia patients.

Methods: Patients were identified using data from the Swedish Hospital Discharge Register since 1987 and from the Outpatient Register since 2001 up to year 2010.

Results: A total of 3064 persons were diagnosed with thalassemia. The incidence was highest, 62.9/100,000 for immigrants from Thailand, followed by Iraqis (47.1/100,000); the rate was 0.7/100,000 among those born in Sweden. The total number of sickle cell anemia patients was 584 and the highest rate of 13.0/100,000 was found for Sub-Saharan immigrants. For thalassemia, 363 of the patients were siblings, while for sickle cell anemia, 180 were siblings.

Conclusions: The data showed that >90% of sickle cell and thalassemia patients were first- or second-generation immigrants to Sweden and the endemic regions for these were the origins of immigrants with the highest incidence. Global immigration provides global challenges to national health care systems.

Keywords

Hemoglobinopathy, recessive disease, immigrants, international health

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Introduction

Sickle cell disease/anemia and thalassemia are hemoglobinopathies which are the most common monogenic diseases in the world: up to 7% of the global population are carriers of an allele for an inherited hemoglobin disorder and 400,000 affected children are born each year.[1] The global number of neonates affected by the abnormal hemoglobin of sickle cell anemia is estimated at 5.5 million at the heterozygous state and 300,000 at the homozygous state with fulminant disease with homozygous hemoglobin S (HbS).[2] Some 80% of these are born in Sub-Saharan Africa (0.7% of local births), while the number of neonates with sickle cell anemia is estimated at 2600 for North America and 1300 for Europe.[3] Some 60,000 children are born with various forms of thalassemia for which beta thalassemia is the most common.[4] The original endemic areas of these diseases were overlapping and included most of Sub-Saharan Africa, the Middle East and India, with pockets in the Mediterranean area (Italy, Greece and North Africa) and Southeast Asia.[1] However, the disease alleles have spread all around the world because of migration. In Sweden, some 100 patients each of sickle cell anemia and thalassemia were reported between 1998 and 2003.[5]

Sickle cell anemia is caused by a point mutation in the beta globin chain, causing glutamic acid to be replaced with

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valine at the sixth position.[3] HbS contains thus two normal alpha globin subunits and two mutant beta chains. Under low-oxygen conditions, HbS has a tendency to aggregate, causing the erythrocyte to assume a sickle shape. The symptoms are characterized by chronic anemia and periodic episodes of pain. This leads to further slowing of circulation, reduction in oxygen tension, more red cell sickling and an eventual blockage of blood vessels and hemolysis, precipitating in a painful crisis.[3] Sickle cell anemia is the most common sickle cell disease which shares many clinical features but constitutes various genotypes, usually including one allele of HbS and a second allele of another beta chain variant.[3] In thalassemia, the stoichiometrically co-ordinated production of globin alpha and beta chains is disrupted because of a dysfunctional globin gene.[6] In alpha thalassemia, the defect is in alpha globin genes of which there are two closely linked copies on chromosome 16. Large deletions encompassing both genes are common in Southeast Asia. In beta thalassemia, there is reduced or absent production of beta globin, encoded by a single gene on chromosome 11. A child born with thalassemia major has two defective alleles for the beta chain gene, resulting in homozygosity for beta thalassemia. The individual with thalassemia minor has only one copy of the defective beta globin gene and he or she is heterozygous for beta thalassemia (also called thalassemia trait). Thalassemia major/intermedia confers a marked deficiency in beta chain production leading to severe anemia with sequelae such as retarded growth, bone deformities, and reduced energy generation—and ultimately death at a young age in the absence of regular blood transfusions. Persons with thalassemia minor have mild anemia or none at all and no treatment is necessary. Both sickle cell anemia and thalassemia are recessive diseases whereby both parents have to be carriers of the disease alleles for the child to be affected; 25% of children are affected by average when both parents are heterozygous carriers, that is, they have sickle cell anemia or thalassemia trait. This is one of the reasons for the endemic presentation of these diseases in the global regions where consanguinity is common.[7] While the standard treatments alleviate symptoms, modern techniques aim at repairing the gene defects by, for example, hematopoietic stem cells.[3,6]

In this article, we provide detailed description on national origins of sickle cell anemia and thalassemia patients diagnosed in Sweden between 1987 and 2010 based on the nationwide hospital discharge and outpatient register. At the onset, we have to emphasize that while the coverage of the diagnosed cases is likely to be close to complete, we have no information on the true incidence because there are no screening programs in place and because some mild forms of these diseases, particularly of thalassemias, would remain undiagnosed. Yet, the medical registers show that by far the largest number of patients were immigrants and most of them originated from the endemic areas of these diseases. As some 15% of the Swedish population (total 9 million) is born outside Sweden and as many recent immigrants arrive from the endemic areas, the results highlight the need to consider national screening programs for these diseases.[8]

Patients and methods

Sickle cell anemia and thalassemia patients were identified using the nationwide Swedish Hospital Discharge Register (1987–2010) and the Outpatient Register (2001–2010). The first diagnosis was included. Information from the registers was linked at the individual level via the national 10-digit civic registration number assigned to each resident in Sweden for his or her lifetime. In the linked dataset, civic registration numbers were replaced with serial numbers to ensure the anonymity of all individuals.

The 10th revision of the International Classification of Diseases (ICD-10) was used to identify disease cases using the following diagnostic codes for thalassemia: alpha thalassemia (D560 as coded in Sweden, while ICD defines the coding as D56.0), beta thalassemia (D561), thalassemia trait (D563), and others (D564-569). For sickle cell anemia, the codes were sickle cell anemia with crisis (D570), sickle cell anemia without crisis (D571), double heterozygous sickling disorders (D572), sickle cell trait (D573), and other (D578). The register data give no information on how the diagnosis was arrived at. In the guidelines of the Swedish National Board of Health and Welfare, the diagnosis of thalassemia is mainly based on microscopic analysis of blood, electrophoresis of hemoglobin, and ethnic/family history of anemia; DNA analysis of specific mutations can also be done, but usually in the context of genetic counseling (http://www.socialstyrelsen.se/ovanligadiagnoser/thalassemi). The guidelines for diagnosis of sickle cell anemia specify analysis of hemoglobin or direct mutation analysis of the hemoglobin gene (http://www.socialstyrelsen.se/ovanligadiagnoser/sicklecellsanemi).

Person-years were calculated from the start of follow-up on 1 January 1987/2001 until diagnosis of the relevant disease, death, emigration, or the end of the study (31 December 2010). All hereditary diseases, newly diagnosed during the follow-up period, were considered, irrespective of their possible kinship. Age-, gender-, region of residence–, immigration status–, and diagnosis subtype–specific incidence rates were calculated for the whole follow-up period. Relative weights used to calculate incidence rates were based on the European Standard Population for 2000. We used SAS version 9.3 for the statistical analyses.

This study was approved by the Ethics Committee of Lund University, Sweden.

Results

According to the Swedish medical registers, 3064 persons had been diagnosed with any type of thalassemia during 1987–2010 (Table 1). Women were more numerous (62%) than men, but the difference was mainly due to those born in Asia; the mean age at first recorded medical contact was 25.2 years for men and 29.7 years for women. Persons born

Table 1. Number of cases and mean age at diagnosis of thalassemia in immigrants, 1987–2010.

Birth country	Men		Women		All	
	No.	Mean age (years)	No.	Mean age (years)	No.	Mean age (years)
Swedish	532	16.4	589	21.9	1121	19.3
Nordic countries	4	37.3	7	44.2	11	42.0
Denmark	1	7.0	2	41.0	3	29.7
Finland	1	57.0	4	48.3	5	30.6
Norway	2	42.5	1	38.0	3	41.0
Southern Europe	34	55.7	39	46.0	73	50.5
France	0		1	24.0	1	24.0
Greece	24	56.3	22	46.4	46	51.5
Italy	5	62.0	7	53.6	12	57.1
Spain	1	77.0	1	57.0	2	67.0
Other Southern European countries	4	39.3	8	39.9	12	39.7
Western Europe	11	38.1	12	38.8	23	38.4
England–Ireland	4	25.8	7	39.4	11	34.5
Germany	6	41.8	4	27.0	10	35.9
Austria	1	65.0	1	81.0	2	73.0
Eastern Europe	30	41.6	68	41.7	98	41.7
Bosnia	4	53.3	9	32.1	13	38.6
Yugoslavia	7	50.6	25	44.8	32	46.1
Romania	7	33.3	12	35.8	19	34.9
Bulgaria	7	36.0	13	42.3	20	40.1
Poland	2	23.5	2	55.0	4	39.3
Hungary	0		3	55.0	3	55.0
Africa	26	35.1	79	33.7	105	34.1
North Africa	7	46.3	26	38.9	33	40.5
Sub-Saharan Africa	19	31.0	53	31.2	72	31.2
North America	3	23.7	4	43.8	7	35.1
Latin America	7	29.1	17	35.0	24	33.3
Chile	2	35.0	7	30.6	9	31.6
Asia	502	30.3	1076	31.9	1578	31.4
Turkey	23	41.5	44	42.3	67	42.0
Lebanon	20	32.1	55	28.5	75	29.5
Iran	108	39.9	178	37.9	286	38.6
Iraq	209	24.7	328	29.8	537	27.8
Syria	20	37.5	48	33.9	68	35.0
Other Arabic countries	22	31.3	28	28.8	50	30.0
Afghanistan	14	27.7	24	29.0	38	28.5
Bangladesh	4	37.3	12	29.2	16	31.2
Pakistan	9	42.3	9	33.8	18	38.1
India	16	35.3	56	23.2	72	25.9
China	5	20.0	29	17.3	34	17.7
Thailand	32	17.7	180	32.8	212	30.5
Vietnam	6	29.3	30	32.6	36	32.1
Philippines	1	12.0	15	46.2	16	44.1
Russia	7	45.7	11	32.0	18	37.3
Others	4	26.0	2	33.5	6	28.5
All	1160	25.2	1904	29.7	3064	28.0

in Asia were the largest group accounting for over a half of all patients; Iraq with 537 persons, Iran with 283 patients, and Thailand with 212 patients were the most common birth countries, after those born in Sweden (1121). Among those born in Sweden, only 179 had a father and 253 a mother born in Sweden (data not shown). For remaining patients, the distribution of parental birth countries resembled that of Table 1, with Iraqi fathers (165) and mothers (156) being the most

Table 2. Number of cases and mean age at diagnosis of sickle cell anemia in immigrants, 1987–2010.

Birth country	Men		Women		All	
	No.	Mean age (years)	No.	Mean age (years)	No.	Mean age (years)
Swedish	164	41.7	182	49.5	346	45.8
Nordic countries	4	42.5	11	54.4	15	51.2
Denmark	2	9.0	2	30.0	4	19.5
Finland	2	76.0	9	59.8	11	62.7
Southern Europe	1	74.0	2	47.0	3	56.0
Greece	1	74.0	0		1	74.0
Other Southern European countries	0		2	47.0	2	47.0
Western Europe	4	57.0	4	55.0	8	56.0
The Netherlands	0		1	68.0	1	68.0
England–Ireland	3	53.0	2	40.0	5	47.8
Germany	1	69.0	1	72.0	2	70.5
Eastern Europe	3	54.3	4	64.5	7	60.1
Yugoslavia	3	54.3	1	72.0	4	58.8
Croatia	0		1	60.0	1	60.0
Poland	0		2	63.0	2	63.0
Africa	45	25.2	83	26.3	128	25.9
North Africa	2	34.0	0		2	34.0
Sub-Saharan Africa	43	24.8	83	26.3	126	25.8
North America	4	28.0	1	2.0	5	22.8
Latin America	1	33.0	4	33.3	5	33.2
Chile	1	33.0	0		1	33.0
Asia	30	24.1	27	30.3	57	27.0
Turkey	1	60.0	2	14.0	3	29.3
Lebanon	5	27.6	8	34.0	13	31.5
Iran	3	42.0	2	25.5	5	35.4
Iraq	14	16.8	8	31.5	22	22.1
Syria	2	7.5	0		2	7.5
India	2	9.0	2	10.0	4	9.5
Russia	0		1	65.0	1	65.0
Others	4	31.3	5	35.8	9	33.8
All	260	36.9	324	41.8	584	39.6

common nationalities. It is noteworthy that the mean diagnostic ages were considerably lower for patients born in Sweden (including only children; 10.5 years for offspring of fathers and 12.0 years for those of mothers) than for those shown in Table 1 (including children and their parents). The diagnostic age for most offspring of African and Asian parents was well below 10 years.

Similar data for sickle cell anemia are available in Table 2. The total number of patients was 584, women only slightly more common than men and the respective mean diagnostic ages of 36.9 and 41.8 years. Persons born in Sweden were the largest group with 346 patients, followed by Sub-Saharan Africans (126). Among Asians, Iraqis (22) and Lebanese (13) were the most common nationalities. Among the 346 Sweden-born patients, only 23 had a father and 45 a mother born in Sweden (data not shown). Offspring of Sub-Saharan African parents were the most common patients group; the mean diagnostic age of all offspring born in Sweden to African and Asian parents was below 5 years.

Table 3 shows the adjusted annual incidence for thalassemia and sickle cell anemia by birth country/region using a defined year as the population estimate. The incidence of thalassemia was highest, 62.9/100,000 for immigrants from Thailand, followed by Iraqis (47.1/100,000); the rate was 0.7/100,000 among those born in Sweden. For sickle cell anemia, the rate was highest 13.0/100,000 for Sub-Saharan immigrants, followed by Lebanese (2.0/100,000). The rate was 0.2/100,000 among those born in Sweden.

Being a genetic disease, thalassemia would be expected to show familial clustering. According to Table 4, 347 patients had an affected sibling by paternal birth country, while the number was 363 by maternal birth country. Iraqi families had the most affected siblings, accounting for one-third of all affected siblings.

Siblings diagnosed with sickle cell anemia accounted for 150 by father's birth country and for 180 by mother's birth country (Table 5). Among these, siblings with Sub-Saharan parents accounted for half of all affected siblings.

Table 3. Incidence rate (per 100,000 person years) of thalassemia and sickle cell anemia in immigrants, 1987–2010.

Birth country	Thalassemia				Sickle cell anemia			
	O	IR	95% CI		O	IR	95% CI	
Sweden	1121	0.7	0.6	0.7	346	0.2	0.1	0.3
Other European countries	205	1.5	1.3	1.6	33	0.2	0.0	0.5
Greece	46	14.3	14.0	14.6	1	0.2	0.0	2.1
Africa	105	9.8	9.7	10.0	128	10.9	10.8	11.1
North Africa	33	14.3	14.0	14.7	2	1.3	0.0	2.6
Sub-Saharan Africa	72	8.7	8.4	8.9	126	13.0	12.8	13.2
North America	7	1.8	1.0	2.5	5	2.3	1.4	3.2
Latin America	24	2.0	1.6	2.4	5	0.3	0.0	1.2
Asia	1578	27.3	27.2	27.3	57	1.1	0.8	1.4
Turkey	67	7.6	7.4	7.8	3	0.9	0.0	2.0
Lebanon	75	16.4	16.2	16.6	13	2.0	1.5	2.6
Iran	286	25.7	25.6	25.9	5	0.3	0.0	1.2
Iraq	537	47.1	47.0	47.2	22	2.2	1.8	2.6
Syria	68	20.5	20.3	20.7	2	3.6	2.2	5.0
Other Arabic countries	50	40.6	40.4	40.9	3	3.6	2.5	4.7
Afghanistan	38	30.2	29.8	30.5	1	1.2	0.0	3.1
Bangladesh	16	14.1	13.6	14.6	0			
Pakistan	18	28.5	28.0	28.9	2	2.1	0.7	3.4
India	72	28.3	28.0	28.5	4	1.5	0.5	2.4
China	34	14.8	14.5	15.2	0			
Thailand	212	62.9	62.7	63.0	1	0.6	0.0	2.6
Vietnam	36	13.7	13.4	14.0	0			
Philippines	16	27.8	27.4	28.3	0			
Russia	18	4.9	4.4	5.4	1	0.2	0.0	2.2
Others	6	1.8	1.0	2.6	9	3.4	2.7	4.0
All	3064	1.5	1.5	1.6	584	0.3	0.2	0.3

O: observed number of cases; IR: incidence rate per 100,000 person years, adjusted for the European Standard Population for 2000; CI: confidence interval.

Table 4. Number of cases and mean age at diagnosis of thalassemia in patients with a sibling history of thalassemia by parental birth country, 1987–2010.

Parental birth country	By father's birth country		By mother's birth country	
	No.	Mean age (years)	No.	Mean age (years)
Sweden	30	8.4	42	13.1
Denmark	2	4.0	0	
Finland	2	10.0	0	
Greece	7	24.7	4	23.3
Italy	2	2.5	2	10.0
England–Ireland	2	7.5	0	
Austria	0		2	34.5
Yugoslavia	7	4.3	6	12.7
Romania	2	8.0	2	8.0
Bulgaria	0		2	12.0
Other Eastern countries	2	28.5	0	
Poland	0		2	10.5
Africa	14	9.4	12	9.3
Turkey	16	11.3	16	11.6
Lebanon	54	8.4	54	8.8
Iran	32	12.2	29	12.2
Iraq	125	9.6	121	9.2
Other Asia countries	50	12.5	69	10.9
All	347	10.2	363	10.7

Table 5. Number of cases and mean age at diagnosis of sickle cell anemia in patients with a sibling history of sickle cell anemia by parental birth country, 1987–2010.

Parental birth country	By father's birth country		By mother's birth country	
	No.	Mean age (years)	No.	Mean age (years)
Sweden	23	33.1	45	39.2
Finland	0		2	41.0
France	1	18.0	1	18.0
Italy	1	5.0	0	
England–Ireland	0		1	0.0
Estonia	1	50.0	0	
Africa	85	6.5	90	7.8
North Africa	2	2.0	2	2.0
Sub-Saharan Africa	83	6.6	88	8.0
Turkey	2	14.0	2	14.0
Lebanon	7	13.6	11	16.0
Iran	4	6.5	5	5.4
Iraq	21	7.1	18	7.6
Other Asian countries	5	16.6	5	5.0
All	150	11.8	180	16.4

Table 6. Number of cases of thalassemia and sickle cell anemia in the Swedish Patient Register, 1997–2010.

Subtypes (ICD-10)	Born in Sweden	Immigrants from Africa	Immigrants from Asia	Immigrants from other countries
Thalassemia				
Alpha thalassemia (D560)	94	9	102	7
Beta thalassemia (D561)	145	26	258	41
Thalassemia trait (D563)	114	6	66	13
Others	710	63	1103	178
All	1063	104	1529	239
Sickle cell anemia				
Sickle cell anemia with crisis (D570)	34	15	10	4
Sickle cell anemia without crisis (D571)	73	56	19	20
Double heterozygous sickling disorders (D572)	88	6	3	8
Sickle cell trait (D573)	104	18	13	14
Others	35	22	10	3
All	334	117	55	49

ICD-10: 10th revision of the International Classification of Diseases.
Note: The total case numbers are lower than all identified patients because disease subtypes were missing for many patients and because the subtype data were available only from year 1997 onwards.

Data were also available for thalassemia and sickle cell types among patients diagnosed in Sweden by birth region (Table 6). Beta thalassemia was the most common specified thalassemia type, particularly among African and Asian immigrants. For sickle cell anemia, sickle cell trait was the most common for people born in Sweden, while sickle cell anemia without crisis was the most common among African and Asian immigrants.

Discussion

The present study showed that although the highest number of sickle cell and thalassemia patients immigrated to Sweden from the endemic areas of these diseases, a smaller number of patients came from almost any other country, indicating the global spread of these diseases. The high population frequency of these hemoglobinopathies was an early puzzle to population geneticists. The old wisdom was that persons with genetic diseases may be seriously handicapped and unable to bear children, whereby disease alleles disappear from the population. However, in inbred populations, the selection against deleterious alleles is not efficient because they are reintroduced into descendants a few generations later. The extraordinary frequency of hemoglobinopathies has been ascribed at least to three reasons.[1] Initially, the diseases became common because heterozygous carriers were

more resistant to malaria infection than non-carriers. Among several possible mechanisms, Plasmodium falciparum may be less invasive in the sickle cell trait. The protection against malaria by a sickle cell allele has been estimated at 80% or more, while that by a beta thalassemia allele may be 50%.[1] Consanguinity has been another contributing factor, and, more recently, the improved survival of patients has increased patient and carrier numbers. These latter two factors are probably at least in part explaining the reasons why hemoglobinopathies appear to decrease slowly in spite of eradication of malaria infections.[1] The tradition of consanguineous marriage continues in many immigrant populations, for instance, among North Africans in France and Belgium, and Turks and other Middle Eastern populations in Germany and the Scandinavian countries.[7]

The advantages of the present study include nationwide coverage of all in- and outpatients and detailed data on the birth country of all individuals. The disadvantage is that the data refer to diagnosed cases which may underestimate true incidence figures by far. However, these data are relevant in describing the patient numbers of these diseases in the Swedish health care system. We showed that >90% of sickle cell and thalassemia patients were first- or second-generation immigrants to Sweden, and the endemic regions for these diseases were the origins of immigrants with the highest incidence. However, both of these hemoglobinopathies have been known in Sweden for decades and cases have been described in native families.[9] A previous publication cites that some 100 patients each of sickle cell anemia and thalassemia were reported to the Swedish Hospital Discharge Register between 1998 and 2003.[5] The present study covered only 7 more years and used additionally the Outpatient Register, but the patient number increased 30-fold for thalassemia and 6-fold for sickle cell anemia.

The population genetics of the disease alleles is of some interest. Even though the sickle cell allele has now spread throughout the world, the haplotype analysis suggests that it arouse only twice, once in Africa and once in India or the Middle East.[1] Thus, the appearance of sickle cell anemia in "native" Swedish families, referred to above, is likely to have origins in historic population mixing, and apparently, the disease allele has nevertheless been imported from the ancient gene pool. For thalassemia mutations, the population history is different and increasing numbers of new alleles are being found; 300 are cited in http://www.patient.co.uk/doctor/thalassaemia-pro. A UK antenatal diagnostics study found 68 different beta thalassemia mutations, and of these, 59 were found in recent immigrants. A total of 40 different alpha thalassemia mutations were found, including all the Southeast Asian and Mediterranean alpha zero thalassemia mutations.[10] As another example, among the more than 45 mutations identified in the beta globin gene in North African countries, there are large regional differences.[4,7] The population histories of the common variants have been traced by haplotype analysis; some alleles originated from central Africa in the Stone Age and migrated from Central West Africa across the then-fertile Sahara to the North. Some other alleles were introduced into North Africa during the Roman period through Italy and Spain.[10]

For thalassemia, the main origins of immigrants to Sweden were Middle East and Southeast Asia, and the incidence rates were highest for Thai (62.9/100,000) and Iraqi (47.1/100,000) immigrants. The first medical contacts were for all patients in their 20s, but because the median age of immigration to Sweden is 24 years, it is likely that most immigrants were aware of their medical conditions before emigration.[8] Accordingly, the second-generation immigrants had their first medical contacts at around age 10 years. The most common specific diagnosis was beta thalassemia which has less severe manifestations than alpha thalassemia. Alpha thalassemia was relatively rare among first-generation immigrant compared to those born in Sweden which is likely to imply selection for emigration by health-based fitness. As there are no known screening programs for thalassemia in Sweden, persons with thalassemia trait were probably diagnosed after they became parents to a homozygous child. The female excess among thalassemia patients may imply that when a homozygous child was born, only mother was registered as a carrier. In Table 6, the largest thalassemia type was "others," which shows the limited diagnostic distinction of thalassemia types among the diagnosed patients in Sweden. This table shows also that thalassemia and sickle cell traits were less numerous than homozygotes, which is against expectations and most likely shows that heterozygous carriers are rarely recorded. For a recessive disease, siblings of heterozygous parents are at risk and the present data on affected siblings follow such expectations. More relevant however is to note that diagnostics work properly among the relatively recent immigrant populations among which Iraqi siblings accounted for one-third of all affected siblings with thalassemia and Sub-Saharans accounted for half of all siblings with sickle cell anemia.

For sickle cell anemia, Sub-Saharan Africa was the main region of origin; the incidence for Sub-Saharans (13.0/100,000) was six times higher than for the next ranking population of Lebanese (2.0/100,000). While the common sickle cell anemia HbS with two mutant beta alleles usually causes disease in early childhood, there are other forms with a milder presentation. These patients are usually double heterozygous for sickle cell mutation and another beta globin mutation, commonly a thalassemia allele.[3] As the first medical contacts in first-generation immigrants were in late 30s, it is likely that they had a mild disease. Again the diagnostic ages in the second-generation immigrants born in Sweden were much lower, suggesting a more aggressive form of sickle cell anemia. Obviously, a severe disease will limit possibilities for emigration, and the relatively much lower incidence of sickle cell anemia compared to thalassemia may be an indication to that effect.

The numbers of affected individuals have increased in Sweden in a short time, and an obvious question is how well

is the Swedish primary health care or that of another host society equipped to meet the demands of these new diseases? This is particularly challenging for the Nordic Countries for which immigration from Africa and Asia is a relatively new phenomenon but has become a considerable portion of all immigration.[5] We reported recently that a large number of familial Mediterranean fever syndrome patients had been diagnosed in Sweden but had received hardly any notice in the medical literature.[11] Similarly, local medical reports on sickle cell and thalassemia are rare. However, the Nordic Countries can learn from countries such as France and the United Kingdom which received the first waves of immigrants from endemic areas of sickle cell anemia and thalassemia after the Second World War. Obviously, the diagnostic and screening methods need to be in place, as for example in the United Kingdom.[12] When a patient presents with anemia in the Swedish primary health care and has an Asian or African ethnic origin, the doctor needs to keep in mind thalassemia and sickle cell anemia. Targeted prevention programs for the reduction of hemoglobinopathies would involve carrier detection, molecular diagnostics, genetic counseling and prenatal diagnosis, but also care of the sick needs to be organized.[13] Organized national prevention programs may be successful even in reducing case numbers, for example, by drawing from the experience in Sardinia or Cyprus. In Sardinia, the number of thalassemia major children born shows a reduction from 1:250 live births to 1:1660 in about 20 years, showing an effective prevention of 85% of the cases.[13]

In conclusion, the present results show that with immigration from Africa and Asia, sickle cell anemia and thalassemia have increased markedly in Sweden. However, it is noteworthy that immigrants from many other countries are also diagnosed with these diseases, yet the country of origin of some of these immigrants may not be the one from where they immigrated to Sweden. The case numbers of these diseases are becoming so large in Sweden that a national program of care and prevention would be needed.

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