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The epidemiology of sickle cell disease in Germany following recent large-scale immigration

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Abstract

Background: The epidemiology of sickle cell disease (SCD) in Germany is currently changing fundamentally with ongoing immigration. Here, we address the challenges resulting from the increased frequency, that is, the morbidity, and mortality of SCD in this population.

Procedure: The number of immigrants with SCD was estimated based on the data of the German central registry of migrants (2007–2015) and published epidemiologic data. Additional data analysis was based on nationwide aggregated data from the diagnosis-related groups' (DRG) statistics of the German Federal Statistical Office.

Results: The total number of patients with SCD among migrants was estimated at 2,016 in 2007 and 3,216 in 2015, thus showing a 60% increase, which was particularly remarkable during 2014 and 2015. The countries of origin included those of West sub-Saharan Africa, followed by Syria, and other countries of the Middle East. In parallel, the number of SCD inpatient treatments increased from 780 in 2002 to 1,340 in 2015. Between 2012 and 2014, 42 patients with SCD died in hospital, mostly at an age of less than 5 years (n = 7) or over 30 years (n = 29).

Conclusion: More than 3,000 patients with SCD are estimated to live among the immigrant population in Germany. In addition, the number of SCD patients of German nationality is not known. The increasing number of inpatient treatments and the death of young children from SCD indicate the need for a general newborn screening program and an increased awareness of this disease among medical practitioners in a country in which SCD used to be rare.

KEYWORDS
epidemiology, Germany, migration, sickle cell disease

1 | INTRODUCTION

Sickle cell disease (SCD) affects multiple organs, resulting in significant morbidity and a reduced life expectancy.[1,2] Patients with SCD may have a median survival of less than 5 years under conditions of limited medical resources.[3] In contrast, medical treatment that includes parent education,[4] vaccinations,[5] antibiotic prophylaxis,[6] hydroxycarbamide,[7] and red blood cell transfusion[8] has resulted in a continuous improvement of survival during childhood.[9] Patients with a human leukocyte antigen (HLA)-matched sibling donor may be cured by allogeneic stem cell transplantation, a procedure that is now recommended as the standard of care.[10]

Neither hemoglobin S (HbS) nor hemoglobin C has been encountered among native Germans.[1] Therefore, SCD is exclusively prevalent among immigrants from endemic areas, especially Africa, Turkey, the Arab countries, and India.[1] Epidemiologic data on SCD in Germany are scarce and have not yet been obtained in an unbiased systematic fashion. The hematology laboratory in Ulm, which specialized in the analysis of hemoglobinopathies in Germany, identified 3,085 patients with SCD between 1971 and 2007.[1] The number of HbS carriers has been estimated at 85,000 in Germany in the year 2000[12] based on the data on global migration. Local newborn screening projects in either urban or mixed urban and rural populations have determined a prevalence of newborns with SCD in the range of 1:2,500 to 1:12,500,[13–15] but do not provide a follow-up of newborns with SCD who have been

Abbreviations: AF, allele frequency; DRG, diagnosis-related groups; HbS, hemoglobin S; HbSS, homozygosity for HbS; HLA, human leukocyte antigen; SCD, sickle cell disease; TCD, transcranial Doppler

identified by screening. The relative rarity of SCD and the lack of systematic centralization of treatment in specialized centers may result in many patients not receiving optimal medical support.

Here, we aim at providing an estimate about the epidemiology of SCD in Germany by analyzing publicly available data that have been gathered from the German Federal Statistical Office. To estimate the change in the number of patients with SCD, we used the data on hospital admissions (available from 2002 to 2015) and the data on immigration (available from 2007 to 2015). In order to give an estimate on morbidity and mortality related to SCD, we made use of detailed data on principal and secondary hospital diagnoses and procedures (available for 2012–2014) and on causes of death (available for 2009–2014).

2 | METHODS

We included publicly available data of the German Federal Statistics Office (Statistisches Bundesamt, Wiesbaden, www.destatis.de) in the analysis.

2.1 | Estimation of the number of patients and newborns with SCD based on data on migration

Data on migration were taken from *Erwerbstätigkeit, Ausländische Bevölkerung, Ergebnisse des Ausländerzentralregisters 2014/2015*, articles 2010200147005 and 2010200157005, www.destatis.de, accessed July 14, 2016. This publication reports the number of people registered in the German central registry of foreigners with, among others, country of origin and age. For all countries or regions with the data on the number of migrants available in the German central registry of foreigners and with estimates on HbS epidemiology available in Piel et al.,[16] the number of patients homozygous for HbS (HbSS) was estimated. The estimation of HbSS frequency was based on Hardy–Weinberg law, calculated as HbS allele frequency to the second. For the estimation of HbSS patient numbers, the HbSS frequency in each population was multiplied by the number of immigrants from the respective country or region. Similarly, to estimate the number of HbSS newborns among the respective migrant population in Germany, the crude birth rate was multiplied by the number of immigrants from the respective country or region.

2.2 | Estimation of the number of patients with SCD based on hospital diagnoses

Data on principal diagnoses of hospital patients were taken from *Gesundheitswesen—Tiefgegliederte Diagnosedaten der Krankenhauspatientinnen und—patienten 2002–2015*, www.destatis.de, accessed June 23, 2016 (for 2002–2014) and November 24, 2016 (for 2015). These publications report the number of cases who have been discharged from inpatient treatment with four-digit diagnosis code according to ICD-10, age groups, gender, and duration of hospital treatment in days. Patients who died in hospital are specified. Data from all hospitals that use the DRG ("diagnosis-related groups") system for calculating costs according to German law KHEntgG §1 are included, but not institutions of psychiatry, psychotherapy, and psychosomatics and no daycare clinics. Patients admitted with the primary diagnosis D57.0 ("sickle cell anemia with crises"), D57.1 ("sickle cell anemia without crises"), D57.2 ("compound heterozygous sickle cell disease"), and D57.8 ("other sickle cell disease") were considered, excluding sickle cell trait. Because admissions, not patients are counted in these statistics, a single patient will generate several cases if admitted repeatedly.

2.3 | Morbidity related to SCD

For all inpatient cases with either principal or secondary diagnosis SCD (D57.0, D57.1, D57.2, D57.8; excluding HbS trait D57.3) in the years 2012–2014, associated diagnoses, medical procedures, and age groups were provided by the Federal Statistical Office. Each diagnosis and procedure can only be generated once per case, but several times for patients who were admitted repeatedly.

2.4 | Mortality related to SCD

First, mortality was estimated based on hospital diagnosis data from 2012 to 2014 (see Section 2.3). Inpatient fatalities (n = 42) that were linked with any of the diagnoses D57.0, D57.1, D57.2, or D57.8 were considered. Concomitant diagnoses were available not on a single-patient level but for all patients with SCD of a certain age group who died in 1 year. If this was a single patient (n = 20), all documented diagnoses were assigned to this patient. If several patients with SCD of one age group had died in a hospital in the same year (eight groups of two patients, two groups of three patients), diagnoses that were most likely related to individual causes of death were assigned according to manual plausibility analysis.

Second, mortality was estimated from the data on cause of death from *Gesundheit. Ergebnisse der Todesursachenstatistik für Deutschland*, www.destatis.de, accessed October 18, 2016. This publication reports the cause of death (as four-digit diagnosis code according to ICD-10) documented by the physician who testified the death, including but not restricted to those who died in hospital.

2.5 | Complications and comorbidity in immigrants with hemoglobinopathies

Immigrants with hemoglobinopathies (n = 32 with SCD, n = 38 with thalassemia major) from the Middle East or Africa who had presented at the departments of pediatric hematology in Berlin (n = 18), Frankfurt (n = 5), Hamburg (n = 23), Heidelberg (n = 11), or Ulm (n = 15) between January 2014 and June 2016 were included in the analysis. Medical charts were retrospectively reviewed for comorbidities: colonization with resistant bacteria requiring isolation in healthcare facilities, hepatitis B or C, HIV, alloimmunization, history of splenectomy, short stature (below third percentile), and low body weight (below third percentile). Additionally, charts of patients with SCD were reviewed for history of stroke, regular red blood cell transfusion, and hydroxycarbamide. Charts of patients with thalassemia major were reviewed for inadequate iron chelation, liver iron content more than

20 mg/g dry weight, heart T2* less than 10 ms, thalassemic face, extramedullary erythropoiesis, and diabetes mellitus.

2.6 | Standard of care for patients with SCD in Germany

Treatment guidelines for SCD in Germany largely reflect guidelines from the United States and the UK. The use of penicillin prophylaxis up to the age of 5 years, annual screening of children and adolescents with transcranial Doppler (TCD), and education of parents with regard to spleen palpation and fever has been recommended for the complete period considered here. However, TCD screening is not available at all institutions treating patients with SCD. Vaccination with pneumococcal conjugated vaccine became available in Germany in 2001 and has been recommended for all infants starting 2006. Up to 2014, the use of hydroxycarbamid was restricted to patients who had suffered severe complications ("hydroxycarbamid is indicated for patients with frequent severe pain crises or recurrent acute chest syndromes"[17]). Current guidelines[18] recommend the use of hydroxycarbamide for all patients with symptomatic SCD starting at the age of 2 years. Allogeneic stem cell transplantation has traditionally been reserved for children and adolescents with the need for chronic transfusions, but it is now recommended as a standard of care for all patients with an HLA-matched sibling donor.[18] To our knowledge, no data are available on the adherence to treatment guidelines.

3 | RESULTS

3.1 | Estimation of the number of patients and newborns with SCD based on data on migration

The total number of patients with SCD in Germany is unknown and cannot be estimated based on population data because reliable information on the migration background of the German population is not available. Thus, we first aimed to estimate the number of SCD patients among immigrants in Germany. Based on allele frequencies in the country of origin that had been reported in the literature,[16] we approximated the proportion of homozygous SCD patients according to the Hardy–Weinberg relation (Table 1). This simple approximation is limited because it does not take into account important but unknown variables such as the differences in life expectancy of HbSS patients, consanguinous or interethnic marriages, preferential migration of HbSS patients seeking medical help, premarital counselling, or induced abortion after prenatal diagnosis. The main region of origin was West Africa, most prominently Nigeria (Table 1; for a more complete table see Supplementary Table S1). This was also the region with the largest absolute increase in the numbers of patients with SCD between 2007 and 2015 (for Nigeria: 490 patients with SCD in 2007, 1,094 in 2015), while the country of origin with the largest relative increase in numbers was Syria (18 patients with SCD in 2007, 229 in 2015). The data also indicate a decline in the number of patients with SCD for some countries of origin such as the Democratic Republic of Congo (−50 patients with SCD from 2007 to 2015), Turkey (−42), and Togo (−21). We cannot ascertain if these groups were no longer registered as immigrants because they had become German citizens or had left the country. In total, an increase in the number of patients with SCD from 2,016 in 2007 to 3,216 in 2015 was estimated, corresponding to an increase of approximately 60% (Fig. 1A).

Analogous results were obtained when we estimated the number of newborns with homozygous SCD among the respective migrant population in Germany based on the assumption that the reported birth rates[16] still apply after migration to Germany. With the data available, this approximation cannot be corrected for variables such as the age of migrants, changes in reproductive behavior after migration, interethnic partnerships between populations of different HbS allele frequencies, premarital counselling, or induced abortion after prenatal diagnosis. With these uncertainties in mind, the number of newborns with homozygous SCD estimated to be born in 2015 was approximately 60% higher than in 2007 (97 vs. 61; Fig. 1B).

3.2 | Estimation of the number of patients with SCD based on hospital diagnoses

Next, we tested if the increase in patients with SCD estimated on the basis of the number and origin of immigrants was reflected by the number of medical treatments for SCD. To this end, we used the inpatient principal diagnoses that are documented as the basis for the calculation of hospital reimbursement. These data were available for the period from 2007 to 2015. During this time, the number of admissions for SCD increased by approximately 60%, from 780 in 2007 to 1,340 in 2015 (Fig. 2A). During the same period, the numbers of admissions for hereditary spherocytosis and phenylketonuria decreased by 33 and 42%, respectively, indicating that the increase in the admissions for SCD was specific. Most patients with SCD were between the age of 1 and 20 years. Only rarely patients older than 40 were treated for the principal diagnosis of SCD (Fig. 2B), indicating that the cohort of patients with SCD in Germany is relatively young compared to countries with a more stable population of SCD patients such as France, the UK, and the United States.[17–19]

In order to assess if the increase in admissions for SCD can be attributed to immigration, we compared the age distribution of patients and immigrants with SCD. Between 2012 and 2014, the increase in admissions for patients with SCD was the strongest for children below the age of 10 and for young adults in the age range between 20 and 35 years (Fig. 2C). This age distribution was mirrored by the number of immigrants at risk of SCD that was highest for young children, presumably having travelled with their parents, and for young adults (Fig. 2D). This strong correlation between the increase in admissions for SCD and immigrants at risk for SCD in the same age groups confirms the expectation that immigration is the main determinant of the recent increase in frequency of SCD in Germany.

3.3 | Morbidity related to SCD

In order to identify the most relevant sequelae of SCD, we analyzed which diagnoses were associated with SCD in inpatients in 2012–2014 (Fig. 3). Importantly, because each individual patient can generate

TABLE 1 Estimates on HbSS patients and HbSS newborns in Germany based on the number of migrants and epidemiologic data from the source regions

Country/region of origin[a]	Migrants in Germany 2015	HbS AF in home country[16]	Population in home country, thousands[16]	Crude birth rate in home country[16]	HbSS patient estimate in migrants in Germany 2015[b]	HbSS neonates estimate in Germany 2015[c]
Nigeria	37,404	0.171	158,255	0.0393	1,094	20
West African region[d]	41,773	0.085	141,025	0.0365	302	11
Cameroon	19,800	0.12	19,957	0.0349	285	7
The Democratic Republic of the Congo	9,299	0.165	67,829	0.0421	253	5
Greece	339,931	0.026	11,194	0.0101	230	6
Syria	366,556	0.025	22,627	0.0219	229	15
Ghana	29,590	0.087	24,339	0.0303	224	7
Togo	10,145	0.125	6,774	0.0310	159	3
Lebanon	37,160	0.049	4,237	0.0149	89	2
Central Africa region[e]	10,292	0.077	4,506	0.0345	61	2
India	86,324	0.023	1,196,940	0.0213	46	3
Kosovo[f]	208,613	0.014	1,800	0.0128	41	2
Turkey	1,506,113	0.005	75,699	0.0169	38	0
France	126,739	0.013	62,618	0.0124	21	1

[a]Only home countries or regions with data on number of migrants in "Ausländerzentralregister" and with estimates on HbS epidemiology in reference 16 that contribute at least 20 HbSS patient are included.
[b]Estimate of HbSS patient numbers based on Hardy–Weinberg law and the number of immigrants from the respective country or region.
[c]HbSS newborn numbers in Germany among the respective migrant population, estimated based on the assumption that the birth rate does not differ between the population in the home country and the migrant population.
[d]Without Ghana, Nigeria, and Togo. HbS allele frequency, population, and birth rate in home region estimated based on epidemiologic data from Benin, Burkina Faso, Cote d'Ivoire, Gambia, Guinea, Guinea-Bissau, Kap Verde, Liberia, Mali, Mauretania, Niger, Senegal, and Sierra Leone.
[e]Without Cameroon and The Democratic Republic of the Congo. HbS allele frequency, population, birth rate, and HbSS neonates in home region estimated based on epidemiologic data from the Central African Republic.
[f]HbS frequency, birth rate, and HbSS neonates in Kosovo estimated based on epidemiologic data from Albania.

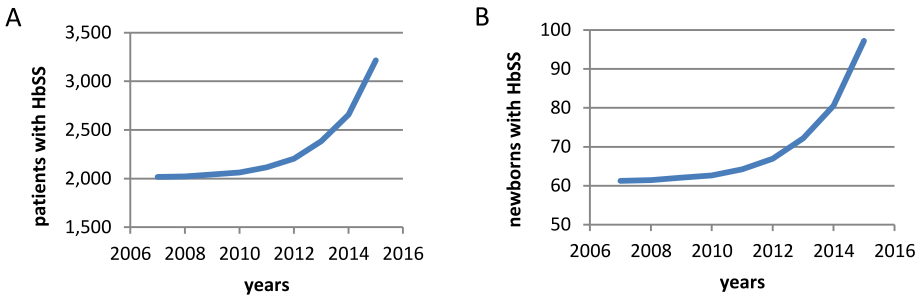

FIGURE 1 Increase in patients and newborns with homozygous SCD among migrants in Germany 2007—2015. (A) The number of HbSS patients was calculated by multiplying HbSS frequency (estimated according to Hardy–Weinberg law) by the number of immigrants from the respective country or region. The curve shows the sum of all estimated HbSS patients among immigrants in Germany. (B) The number of HbSS newborns among migrant populations in Germany was estimated based on the assumption that the birth rate does not differ between the population in the home country and the migrant population. The curve shows the sum of all estimated HbSS newborns among immigrants in Germany

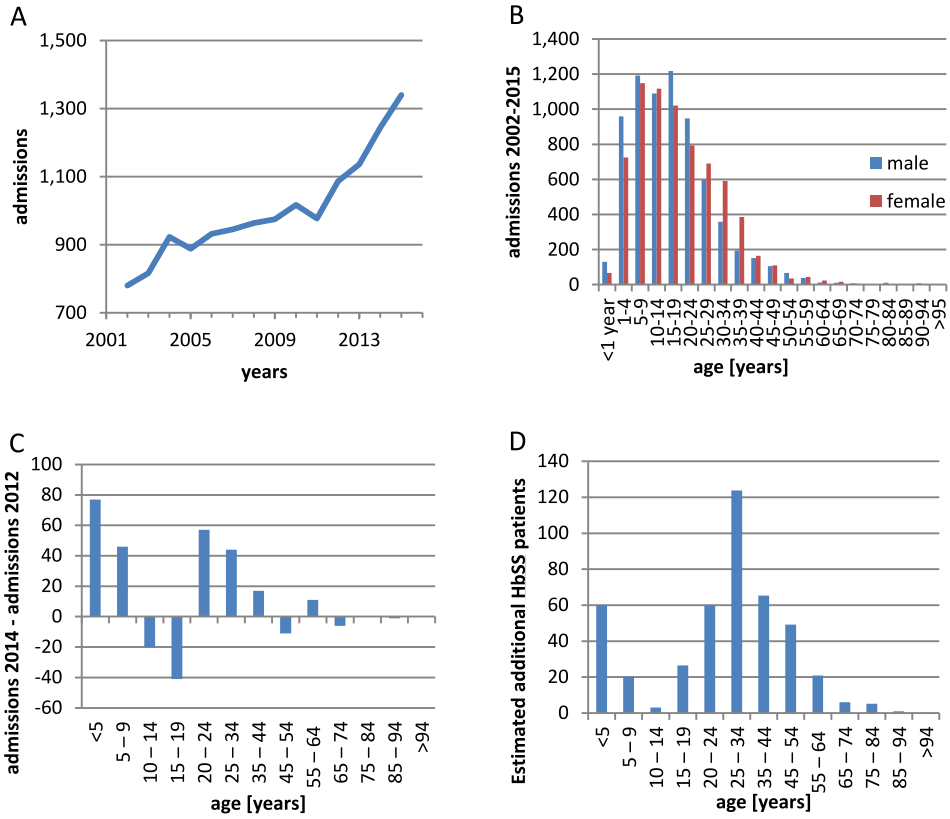

FIGURE 2 Increase in patients treated for SCD in Germany 2002—2015. (A) Inpatient treatment cases with principal diagnosis D57.0, D57.1, D57.2, or D57.8 (including homozygous and compound heterozygous SCD, but excluding sickle cell trait). (B) Distribution of age and sex in all inpatients treated for principal diagnosis SCD (D57.0, D57.1, D57.2, or D57.8) 2002–2015. The increase in inpatient treatment for SCD is correlated with immigration from regions with high SCD prevalence. (C) Increase in inpatient treatment cases with principal or secondary diagnosis D57.0, D57.1, D57.2, or D57.8 (including homozygous and compound heterozygous SCD, but excluding sickle cell trait) from 2012 to 2014 according to age groups. (D) Estimated increase in the number of patients with homozygous SCD, calculated as described in Table 1, between 2012 and 2014 according to age groups

several hospital admissions, we can estimate only relative, not absolute numbers of patients with comorbidities. The most characteristic age distributions were observed for ischemic stroke and priapism, with stroke affecting mainly children of young school age (Fig. 3C) and priapism young men between 15 and 25 years of age (Fig. 3D). Sepsis and pneumonia (which is usually coded for acute chest syndrome) largely recapitulate the age distribution of patients with SCD (Figs. 2B and 3A and 3B). In contrast, the age distribution for cholelithiasis was shifted toward an older age (Fig. 3E). As expected, leg ulcers and renal failure were characteristic of patients older than 35 years (Figs. 3F and 3G). In total, 13 admissions for malaria (B50–B54) were documented in the age groups of 1–15 years and 35–50 years. Most likely, the

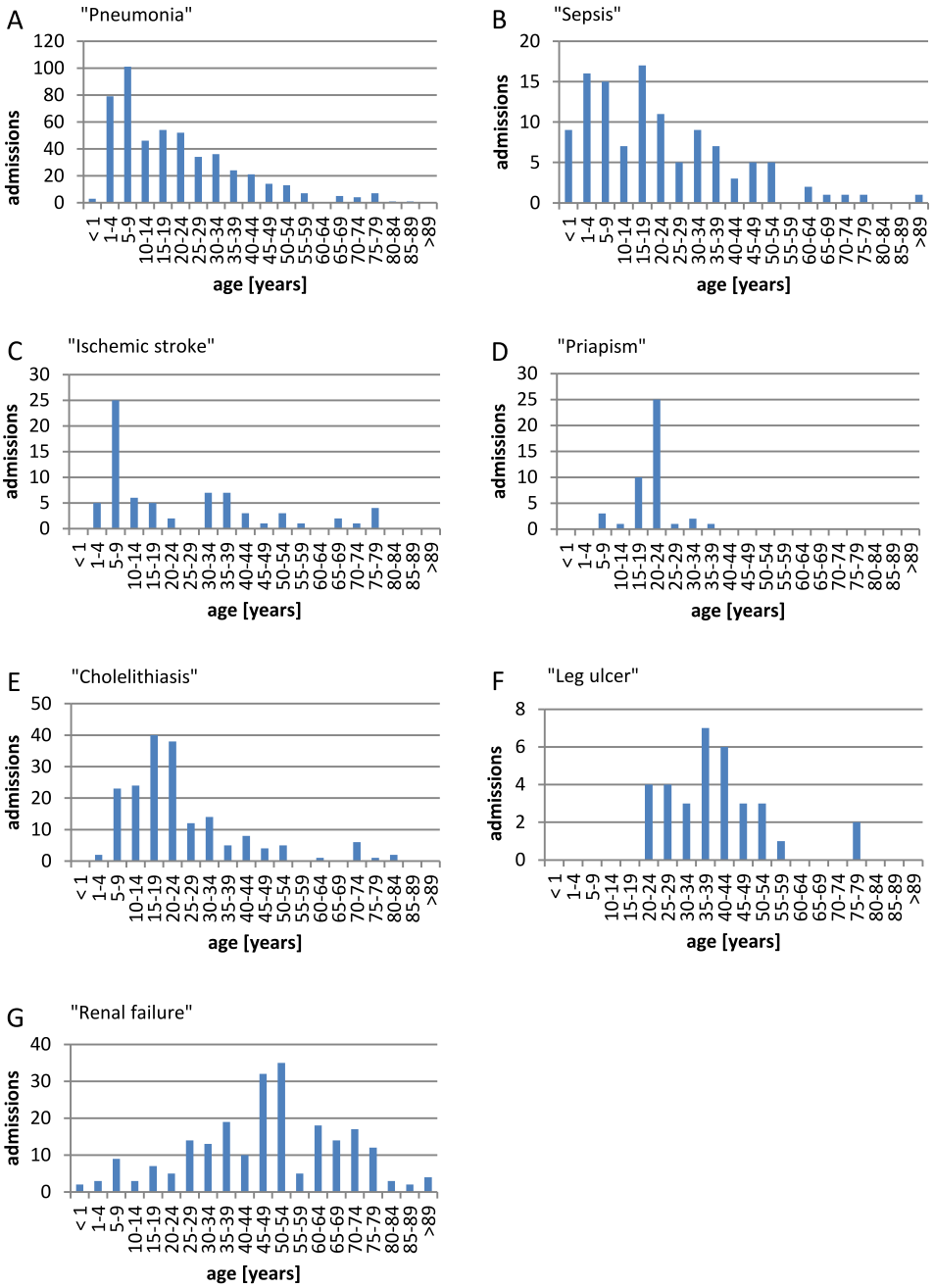

FIGURE 3 Complications of SCD. Typical complications of SCD that were treated either as principal or as secondary diagnosis from 2012 to 2014 according to age groups. (A) pneumonia (J12–J18), (B) sepsis (A39–A41), (C) ischemic stroke (I63–I67), (D) priapism (N48.3), (E) cholelithiasis (K80), (F) leg ulcer (I83, I87.21, I70.24, I70.25, or L97), and (G) renal failure (N17–N18). Because each patient can generate more than one case, the number of patients is less than the number of admissions

most frequent cause of admission was painful crisis. However, because there is no separate diagnosis code for this complication, we cannot comment on the frequency and age distribution of painful crises.

Medical procedures that are documented by hospitals allow for an alternative view on comorbidities of SCD. While red blood cell transfusion and exchange transfusion mirror the overall age distribution of patients with SCD (Figs. 4A and 4B), hemodialysis and joint replacement are almost exclusively documented in adult patients (Figs. 4E and 4F). Typical procedures during childhood and adolescence are splenectomy and allogeneic stem cell transplantation (Figs. 4C and 4D). The former has been recommended as a "standard of care" procedure in patients with SCD who have an HLA-matched sibling donor.[10,20] Consequently, the number of allogeneic transplants for the indication SCD has increased from an average of 8 per year in the years 2011–2013 to 15 in 2014 and 22 in 2015.[21]

3.4 | Mortality related to SCD

In order to estimate the number of patients dying from SCD, we made use of two different statistical data sets. Hospital inpatients having

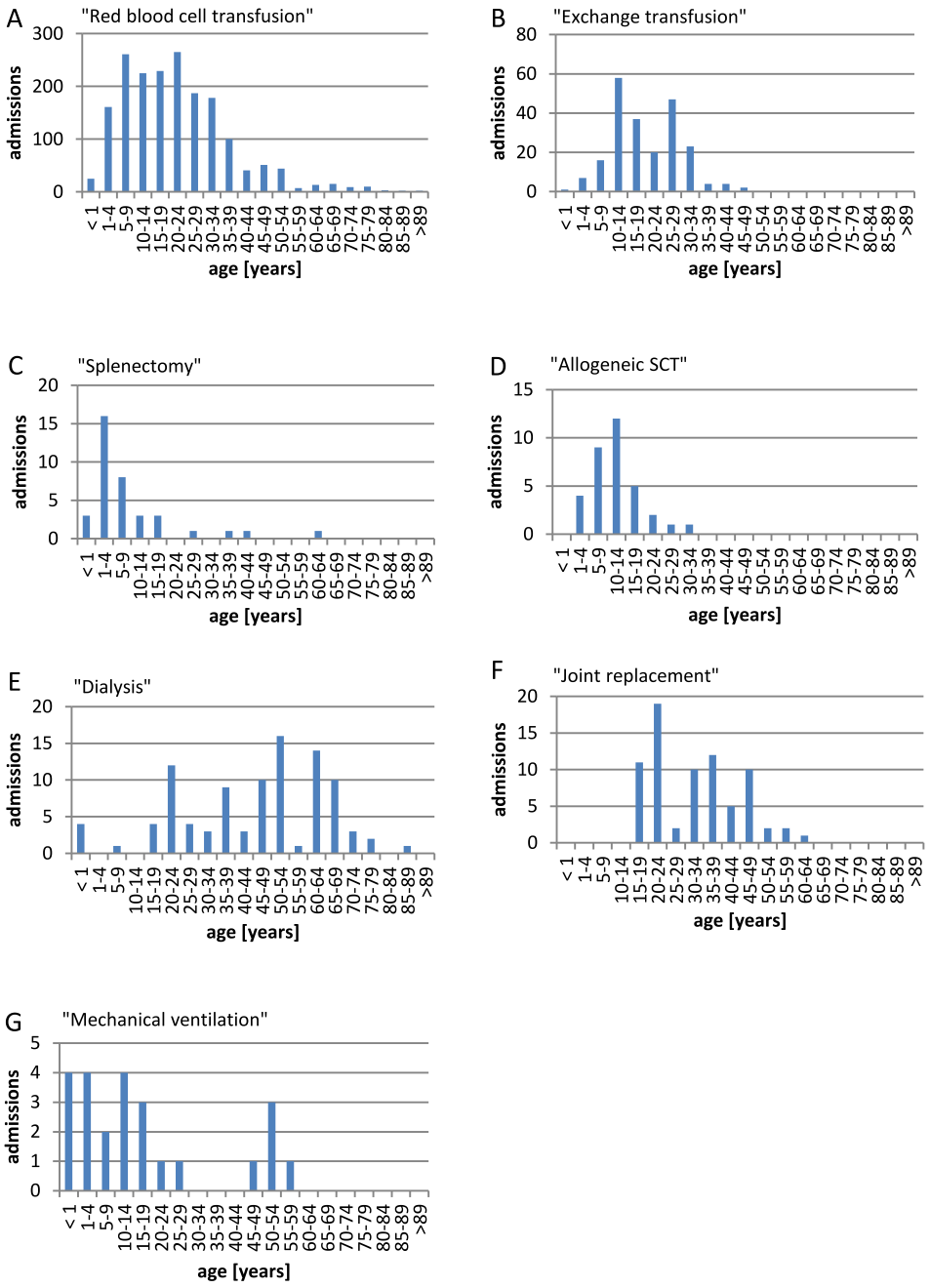

FIGURE 4 Procedures in SCD. Typical procedures in the treatment of SCD from 2012 to 2014 according to age groups. (A) Red blood cell transfusion (8-800.c), (B) exchange transfusion (8-801), (C) splenectomy (5–413), (D) allogeneic SCT (8-805.2–8–805.5, 5-411.2–5-411.5), (E) hemodialysis and hemofiltration (8-853–8-857), (F) joint replacement (5-82), and (G) mechanical ventilation (8-71)

died with either principal or secondary diagnosis SCD in the period 2012–2014 (n = 42) mainly belonged to the age groups below 5 and above 30 years (Fig. 5A), the mean age of death was 41.2 years. The most frequent causes of death likely related to SCD were sepsis (n = 13, 2 in the age group between 1 and 5 years, 11 in patients older than 20 years), pneumonia/chest syndrome (n = 6), heart failure (n = 3), thromboembolic events (n = 2), and pulmonary hypertension (n = 1). One patient (age group 5–9 years) died of complications related to allogeneic stem cell transplantation. In 13 patients, the causes of death were not clearly related to SCD (in children: cystic fibrosis in two patients, extreme prematurity, sphingolipidosis; in adults: neoplasms in four patients, AIDS, endocarditis, myocardial infarction, cholangitis after surgery, trauma).

The age distribution that was found in patients with SCD dying in hospital was confirmed by the statistics on the cause of death that is based on the diagnosis made by the physician who had testified the death, including all deceased irrespective of the place of death. These data were available for the period from 2009 to 2014 and again showed a bimodal distribution, with a first peak below 5 years of age and a second peak around 40 years of age (Fig. 5B). In a total of

FIGURE 5 Patients with SCD are at risk of early death. (A) Age distribution of patients who died 2012–2014 in hospital with SCD (D57.0, D57.1, D57.2, or D58.8, excluding sickle cell trait) as principal or secondary diagnosis. (B) Age distribution of fatalities (2009–2014) whose main cause of death was considered to be SCD by the physician who testified the death

42 patients with a mean age of 38.7 years, the main cause of death was certified to be SCD. Discrepancies between the two statistics may be caused by different periods and by the proportion of deaths not attributed to SCD. The mean age of death of around 40 years is reflected by the strong decline in admissions between the age of 20 and 50 years (Fig. 2B).

3.5 | Complications and comorbidity in immigrants with hemoglobinopathies

In order to correlate statistical data with clinical practice, we collected data on immigrants from the Middle East or Africa who had presented in our departments between January 2014 and June 2016 (Supplementary Table S2). Patients with SCD were at a high risk of treatment-related complications, in particular infections with hepatitis, colonization with resistant bacteria, and alloimmunization. Nine of 32 and 6 of 31 evaluable patients with SCD had a body weight and height below the third percentile for the German population, respectively. All patients from Syria, but not from Africa, had received regular transfusion without clear indication according to the current treatment guidelines.[20,22] Patients with thalassemia major suffered from similar problems, but additionally from complications of thalassemia due to insufficient treatment. Fifteen of 37 patients had a thalassemic facies or a widened diploe. Eleven and 7 of 36 evaluable patients with thalassemia major had a body weight and height below the third percentile for the German population, respectively. In summary, complications in immigrants with hemoglobinopathy are much more common than in patients who had been treated in Germany before.[23,24]

4 | DISCUSSION

Our analyses complement available data on the frequency and manifestation of SCD in Germany.[11,13–15,23] These data show a steady increase in the number of inpatient treatments for SCD, which is paralleled by immigration from regions of high SCD prevalence. While we can roughly approximate the number of patients with homozygous SCD among immigrants to be in the range of 3,000, Germans with SCD, mainly of African or Turkish ancestry, have been numbered around 1,000 in earlier publications.[23]

The sharp decrease in hospital admissions after the age of 19 years (Fig. 2B) is in contrast to observations from the United States[25] and indicates that most patients with SCD living in Germany are younger than 25 years. This may be partially explained by the relatively young age of immigrants from regions of high SCD prevalence, such as Africa (mean age 32 years in 2015) or Syria (26 years). Possibly, children with SCD are overrepresented in these groups because families affected by SCD may be driven to migrate in the search for medical support. Additionally, the reduced life expectancy of SCD patients in the countries of origin and the physical strength required to manage the travel under most difficult circumstances likely reduces the number of older patients arriving in Germany. The mean age of death by SCD was estimated to be around 40 years by two independent surveys (Fig. 5). Because the age distribution of patients with SCD is determined by migration, because all available statistics on causes of death are most likely incomplete, and because the likelihood of non-SCD-related mortality increases with increasing age, the mean age of death is not a valid approximation of the life expectancy of patients with SCD. Nevertheless, the overrepresentation of young patients may contribute to the relatively low number of fatalities that were reported before 2015. Moreover, we predict that we may have to face a steep rise in the fatalities attributable to SCD during the next years, while the current patients with SCD approach the age when complications such as renal insufficiency or pulmonary hypertension become threatening.

Patients with SCD in Germany include many ethnicities (Table 1). Especially the proportion of patients with SCD who are not of African ancestry[23] is higher than that in North America or the UK.[26,27] Nevertheless, the complications that affect patients with SCD in Germany are qualitatively similar to those in other, well-characterized groups of patients.[1,28,29] An important difference between SCD in Germany and in other developed countries is the lack of a newborn screening program for SCD in Germany. This may partially explain the mortality in the age group below 5 years that has almost disappeared in other countries that have introduced a newborn screening.[9,30] Remarkably, 3 of 10 children with SCD who died before reaching the age of 15 had

suffered from other genetic disorders that are inherited in an autosomal recessive manner (cystic fibrosis in two patients, sphingolipidosis in one). We do not know if this coincidence is merely by chance or if it is due to consanguineous parenthood among immigrants from regions with a high prevalence of the HbS trait.

Our study suffers from several limitations, mainly because none of the data sources presented here was intended to provide data on the epidemiology of SCD. While we can approximate the relative change in numbers of patients with SCD based on both hospital diagnoses and on migration data, we cannot directly arrive at absolute numbers of patients with SCD because German patients with SCD are not covered by any statistics. Similarly, the fatalities caused by SCD that are documented in the available databases are most likely underestimated. Practitioners that certify the cause of death may not be aware of complications related to SCD even if this diagnosis has been made before. In addition, sudden death due to, for example, pneumococcal infection may not be recognized as related to SCD in children who were not diagnosed before. Further, the lack of exposure to SCD of many medical practitioners in Germany may contribute to a higher fatality rate because of delayed diagnosis and delayed implementation of appropriate treatment.

In 2016, we thus initiated a German registry for SCD, which will first provide more detailed and prospective data on the epidemiology of SCD in Germany that will help political decision makers to appreciate and address the new challenge as one aspect of the more general issues that arise with mass immigration into this country. Second, the registry is intended to improve the quality of medical care by providing a network that can be accessed by physicians, patients, and their families for advice. Further, with the already documented high incidence of SCD in the newborn population, Germany clearly needs a newborn screening program for SCD and to implement already existing guidelines by training of healthcare staff and parents. While some of these goals have been achieved for pediatric SCD patients in the last years, the care for adult patients with SCD remains a particular concern that will become even more urgent while our patients grow older. The transition to adult medicine can be facilitated by patient training, but requires dedicated physicians who are trained and experienced in the medical problems of adult patients with SCD.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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