Diabetes care in pediatric refugees from Africa or Middle East: experiences from Germany and Austria based on real-world data from the DPV registry

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Abstract

Objective: With increasing migration to Europe, diabetes diagnosis and treatment of refugees became challenging. To describe the current experience with pediatric refugees in Germany and Austria.

Design and Methods: 43,137 patients (<21 years) with type 1 diabetes from the diabetes patient follow-up registry (DPV) were studied and divided by refugee status into patients born in Middle East ($n = 365$) or Africa ($n = 175$) and native patients (child and parents born in Germany/Austria; G/A: $n = 42,597$). Groups were compared using multivariable regression adjusted for age, sex and diabetes duration (SAS 9.4). In refugees the first year after arrival was studied, and for native children the most recent year of care.

Results: After adjustment, HbA1c was highest in refugees (1. ME and 2. AFR vs 3. G/A: 72.3 ± 1.0 and 75.0 ± 1.4 vs 66.0 ± 0.1 mmol/mol, 1 vs 3: $P < 0.001$ and 2 vs 3: $P < 0.001$) and microalbuminuria (9.9 and 13.6 vs 6.5% , 1 vs 3: $P = 0.039$ and 2 vs 3: $P = 0.002$) was more prevalent. African children experienced severe hypoglycemia (17.8 ± 4.3 and 25.4 ± 8.7 vs 11.5 ± 0.3 per 100 patient years, 1 vs 3: $P > 0.05$ and 2 vs 3: $P = 0.045$) significantly more often, whereas hypoglycemia with coma (5.1 ± 1.1 and 4.1 ± 1.6 vs 2.6 ± 0.1 per 100 patient years, 1 vs 3: $P = 0.006$ and 2 vs 3: $P > 0.05$) and retinopathy (2.1 and n/a vs 0.2% , 1 vs 3: $P < 0.001$) were significantly more common in children from Middle East compared to natives. Insulin pumps were used in a markedly larger proportion of native patients (7.4 and 13.2 vs 43.0% , 1 vs 3: $P < 0.001$ and 2 vs 3: $P < 0.001$).

Conclusions: A relevant number of pediatric refugees with type 1 diabetes are treated in German/Austrian diabetes clinics. Refugee children, parents and caregivers are faced with several problems in diabetes therapy and outcome that should be addressed more intensively by pediatric diabetes teams.

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Introduction

Due to the increasing number of refugees in Western and Central Europe, countries such as Germany and Austria are faced with a challenge politically, socially, and also medically. With increased migration, the number of refugees from Africa (AFR) or the Middle East (ME) with diabetes is on the rise. The majority are still coming from Syria, Iraq and Afghanistan (1), although another flow of refugees exist from North Africa, mainly the Maghreb states. Diabetes health care teams and the national health care systems are faced with the changing population structure and the increasing cultural diversity that leads for example to language problems and challenges diabetes care.

The right to health care for refugee children is codified in the UN Convention on the Rights of the Child (UNCRC) (2). It states that child refugees should have access to health services equivalent to those of the local population in the host country (2). A recent publication however found that most European countries (80%) do not entitle migrant children to the care codified in the UNCRC (3). In our previous DPV analyses, rate of insulin pump therapy was reported to be roughly half among pediatric type 1 diabetes patients with Turkish background compared to those without migration background (4). In addition, depending on the region of origin, additional differences in diabetes therapy and outcome were present (5).

Refugee children with non-infectious chronic diseases such as type 1 diabetes and their families are in an exceptional situation after arrival in the host country. Despite laws and agreements regulating the access to health care, prejudice and uncertainty toward the social interaction with refugees exist. Real-world registry data provide a unique source to study current diabetes practice and experience among pediatric refugees. The aim of this study was to investigate diabetes care in the first year of stay in Germany/Austria among pediatric refugees from the ME and Africa and to compare the results to native patients in order to describe current diabetes treatment and outcome.

Methods

Data collection

Data were collected during routine care and retrieved from the standardized diabetes patient follow-up (DPV; 'Diabetes-Patienten-Verlaufsdokumentation', www.d-p-v.eu), a German/Austrian/Luxembourgian and

Swiss database for people with diabetes. Anonymized data are transmitted twice a year from participating health care facilities, using the DPV software, to Ulm, Germany, for central analysis (5, 6). Implausible and inconsistent data are reported back to the centers for correction. 182 German diabetes centers and 11 centers from Austria taking care of pediatric refugees from Africa and/or the ME contributed data to this analysis. The Ethical Committee of Ulm University has approved the DPV initiative and the institutional review boards of each participating clinic approved the anonymized data collection.

Patients

We initially included 45,400 patients (<21 years) with type 1 diabetes ($n=43,137$; 95.0%), type 2 diabetes ($n=774$; 1.7%) or other specific types of diabetes ($n=1489$; 3.3%) in our analysis. Patients' medical data were documented between January 1995 and March 2018. Both patients and parents are asked for their country of birth. To group patients by refugee status, country of birth was used. Children born in ME (Syria, Afghanistan, Iran and Iraq) or Africa were classified as refugees. In Africa, all countries were considered; Morocco (25.4%), Egypt (12.7%), Eritrea (9.0%), Libya (7.9%), Somalia (7.9%), Ethiopia (5.8%) and Tunisia (5.3%) contributed more than 5% of African refugees, respectively. Native patients were defined as child and both parents born in Germany or Austria. In refugees, the first year of care after arrival in the host country was studied, for native patients the most recent year of care. In case of multiple visits per patient per year, data were aggregated.

Diabetes care processes and outcomes

Anthropometry

To adjust for age and sex, body mass index standard deviation scores (BMI-SDS) were calculated using national reference data from the German Health Interview and Examination Survey for Children and Adolescents (KiGGS) (7). As there are no reliable reference data for children from Africa or the ME, the KiGGS data were also applied for refugee children.

Metabolic control

Glycemic control was evaluated by HbA1c. In order to adjust for differences among laboratories, HbA1c data were mathematically standardized to the DCCT reference

range of 20.77–42.62 mmol/mol (4.05–6.05%) using the multiple of the mean (MOM) method (6).

Treatment modalities

Insulin treatment regimen was classified as conventional insulin therapy (CT; 1–3 daily injection time points), intensive insulin treatment (ICT; 4–8 daily injection time points) or insulin pump therapy (CSII). Daily insulin dose per kilogram bodyweight and daily number of SMBG were studied.

Acute diabetes complications

Diabetic ketoacidosis was defined as blood pH value <7.3 or a clinical diagnosis associated with inpatient care. Severe hypoglycemic episodes were defined as self-reported cognitive impairment, being unable to take glucose, glucagon or other corrective actions without help from others. Hypoglycemia with coma was defined as a sub-group of severe hypoglycemia associated with loss of consciousness or seizure.

Long-term diabetes complications

Microalbuminuria was defined as at least two positive urine tests (spot urine, overnight collection or 24-h urine samples) within 1 year. Diabetic retinopathy (non-proliferative or proliferative) was diagnosed if patients had at least one abnormal eye examination within the respective year of study. Arterial hypertension was defined as taking antihypertensive medication and/or elevated blood pressure above the 95th percentile of the KiGGS reference population (8). Dyslipidemia was diagnosed if patients were taking lipid-lowering drugs or had permanently (defined by at least two consecutive measurements) increased total cholesterol, low-density cholesterol, triglycerides (TGs) or permanently decreased high-density cholesterol. Cut-off values were as follows: total cholesterol >5.2 mmol/L, LDL >3.4 mmol/L, HDL <0.9 mmol/L and TG >1.5 mmol/L. Moreover, number of inpatient admissions per 100 patient years was studied.

Statistical analysis

Statistical analysis was performed using the SAS statistical software package (version 9.4; SAS Institute Inc.).

All measures are presented as median with interquartile range (IQR) or as percentage. For unadjusted group comparison of continuous variables, Kruskal–Wallis test was used. Binary variables were compared by χ^2 test. To adjust for confounding effects of sex, age and diabetes duration, multivariable regression analyses (linear regression for continuous variables, logistic regression for binary outcomes and negative binomial regression for number of events) were applied. The method of Tukey–Kramer was used to adjust for multiple comparisons. To investigate the impact of the region of diabetes manifestation on treatment regimen in type 1 diabetes patients, a sub-analysis on 437 refugees with additional information on the place of diabetes manifestation, i.e. abroad prior to migration vs after migration to Germany/Austria, was performed. A two-sided *P* value <0.05 was considered statistically significant.

Results

Among the pediatric patients studied, we identified 584 children (1.3%) with African or Middle Eastern migration background, here defined as refugees. The majority of refugee children from the ME ($n=272$, 67.3%) immigrated between 2014 and 2018, whereas most refugees from Africa ($n=137$, 72.5%) immigrated prior to 2014. More than half of refugee children from ME (73.4% out of $n=338$) or Africa (56.7% out of $n=120$) with available information on the place of diabetes manifestation were diagnosed with diabetes in their home country prior to the migration to Germany or Austria.

Data on type 2 diabetes or other specific types of diabetes

Although a relevant number of pediatric patients with type 2 diabetes ($n=774$) or other specific types of diabetes ($n=1489$) has been documented in the database, the number of refugee children born in Africa or the Middle East with type 2 diabetes (AFR: 0.9%, $n=7$; ME: 1.7%, $n=13$) or other specific types of diabetes (AFR: 0.3%, $n=5$; ME: 1.3%, $n=19$) was low. Hence, no statistical evaluation of diabetes care process and outcome was performed. Table 1 summarizes the various causes of other specific types of diabetes documented for the refugees studied. Six out of 24 patients had MODY diabetes (Table 1).

Table 1 Different causes of other specific types of diabetes in refugee children from Africa or Middle East.

	Africa (n = 5)	Middle East (n = 19)
MODY diabetes	1	5
Diabetes in thalassemia	–	4
Diabetes in down syndrome	1	2
Diabetes due to other genetic diseases	2	2
Mitochondrial diabetes	–	3
Diabetes due to diseases of the exocrine pancreas	–	2
Drug-induced diabetes	1	–
Not otherwise specified	–	1

Data on type 1 diabetes

Among the refugee children studied, 539 patients had type 1 diabetes (AFR: $n=175$, ME: $n=365$). Demographics and the average number of visits per year are summarized in Table 2, stratified by refugee status. The majority of patients both refugees and natives have been seen by the diabetes care team at least four times a year (ME vs AFR vs G/A: 71.0 vs 70.3 vs 73.6%). Compared to native children, refugees from the ME or Africa were younger and had shorter diabetes duration, with lowest values in children with African background. After adjustment for age, sex and diabetes duration, BMI-SDS was similar between native children and refugees.

Metabolic control and diabetes outcome

Table 3 summarizes results of multivariable regression analyses with adjustments for age, sex and diabetes duration. Glycemic control differed significantly among groups, with highest HbA1c levels in refugees from Africa and lowest values in native children.

Compared to native patients, acute diabetes complications such as severe hypoglycemia were more common in refugees with African background, whereas refugees from the ME experienced hypoglycemia with coma significantly more often. DKA did not differ among groups.

With regard to long-term diabetes complications, microalbuminuria was present in refugees significantly more often compared to natives, whereas retinopathy was more common in children with Middle Eastern refugee status. Frequencies of dyslipidemia and hypertension did not differ among groups. Overall, the number of hospital admissions was higher in refugees (Table 3).

Treatment regimen

Treatment modalities differed between groups, with markedly higher use of insulin pump therapy in native children compared to refugees from either Africa or the ME. Intensive insulin therapy was the most common treatment modality in refugees (Fig. 1). Refugee children from the ME required more insulin per kilogram body weight compared to refugees from Africa or native patients, although the difference between refugees from the ME and Africa was of minor clinical relevance (Table 3).

Interestingly, the region of diabetes manifestation seemed to have an impact on treatment modality. Although not significant after adjustment for age, sex and diabetes duration, children with Middle Eastern refugee status used insulin pump therapy more often if diabetes was diagnosed in Germany or Austria compared to children who were diagnosed with diabetes in their home country prior to migration (12.0 vs 5.4%, $P=0.09$). This is in contrast to refugees from Africa, where insulin pump therapy was documented more frequently in children

Table 2 Demographics of pediatric type 1 diabetes patients, stratified by refugee status. Data are expressed as non-adjusted median with interquartile range or as percentage, except for BMI-SDS. Due to multiple comparisons, P values were adjusted using false discovery rate algorithm.

	Refugee status			P value		
	1. ME (n = 365)	2. AFR (n = 175)	3. Native (n = 42,597)	1 vs 2	1 vs 3	2 vs 3
Girls, %	41.9	41.7	46.6	ns	ns	ns
Age, years	11.8 (8.2–15.3)	12.4 (8.5–15.8)	15.6 (12.0–17.5)	ns	<0.001	<0.001
Diabetes duration, years	1.8 (0.4–6.0)	0.6 (0.3–3.6)	5.2 (2.3–8.9)	0.006	<0.001	<0.001
BMI-SDS*	0.21 $\pm$ 0.05 (n = 359)	0.27 $\pm$ 0.07 (n = 171)	0.27 $\pm$ 0.01 (n = 41,960)	ns	ns	ns
1 visit per year, %	14.5	10.8	7.3	ns	<0.001	ns
2 or 3 visits per year, %	14.5	18.9	19.1	ns	ns	ns
≥ 4 visits per year, %	71.0	70.3	73.6	ns	ns	ns

*Adjusted mean $\pm$ S.E.M., based on multivariable linear regression model with adjustment for age, sex and diabetes duration; P value adjusted for multiple comparisons using the method of Tukey–Kramer.

AFR, Africa; BMI-SDS, body mass index standard deviation score; ME, Middle East.

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Table 3 Metabolic control and diabetes complications in pediatric type 1 diabetes patients, stratified by refugee status.

	Refugee status			P value		
	1. ME (n = 365)	2. AFR (n = 175)	3. Native (n = 42,597)	1 vs 2	1 vs 3	2 vs 3
HbA1c, mmol/mol	72.3 ± 1.0 (n = 361)	75.0 ± 1.4 (n = 174)	66.0 ± 0.1 (n = 41,826)	ns	<0.001	<0.001
HbA1c, %	8.77 ± 0.09	9.01 ± 0.13	8.19 ± 0.01			
Insulin dose, IU/kg*day	0.992 ± 0.016 (n = 358)	0.917 ± 0.023 (n = 172)	0.865 ± 0.001 (n = 41,837)	0.02	<0.001	ns
SMBG, per day	4.29 ± 0.12 (n = 323)	4.46 ± 0.18 (n = 156)	4.88 ± 0.01 (n = 38,876)	ns	<0.001	ns
Severe hypoglycemia, per 100 pat. yrs.	17.8 ± 4.3	25.4 ± 8.7	11.5 ± 0.3	ns	ns	0.045
Hypoglycemia with coma, per 100 pat. yrs.	5.1 ± 1.1	4.1 ± 1.6	2.6 ± 0.1	ns	0.006	ns
DKA, per 100 pat. yrs.	3.0 ± 1.1 (n = 346)	3.7 ± 1.9 (n = 160)	2.0 ± 0.1 (n = 41,554)	ns	ns	ns
Hypertension, %	26.1	26.8	30.6	ns	ns	ns
Dyslipidemia, %	28.7	31.4	25.3	ns	ns	ns
Microalbuminuria, %	9.9	13.6	6.5	ns	0.039	0.002
Retinopathy, %	2.1	n/a	0.2	n/a	<0.001	n/a
Inpatient admissions, per 100 pat. yrs.	77.0 ± 5.0	79.1 ± 7.4	53.1 ± 0.4	ns	<0.001	<0.001

Adjusted means with s.e.m. from multivariable regression models with adjustments for age, sex and diabetes duration. The method of Tukey-Kramer was used to adjust for multiple comparisons.

AFR, Africa; DKA, diabetic ketoacidosis; ME, Middle East; pat. yrs., patient years; SMBG, self-monitoring of blood glucose.

with diabetes diagnosis prior to migration to Germany/Austria, although statistical significance is lacking (13.7 vs 5.3%, $P=0.18$). Intensified insulin therapy was the most common treatment in all groups, independent from the place of diabetes diagnosis (diabetes diagnosis in Germany/Austria vs diabetes diagnosis prior to migration, ME: 76.6 vs 85.4%, $P=0.15$; AFR: 88.1 vs 78.5%, $P=0.22$).

Figure 1

Treatment regimen in pediatric type 1 diabetes patients, stratified by refugee status. AFR, Africa; CSII, continuous subcutaneous insulin infusion; CT, conventional insulin therapy; G/A, Germany/Austria; ICT, intensified insulin therapy; ME, Middle East. Adjusted proportions from multivariable regression models with adjustments for sex, age and diabetes duration. ** $P < 0.001$ and * $P < 0.01$ for the comparison between refugees (ME/AFR) and native children (G/A).

In African refugees, conventional insulin therapy was documented slightly more frequently if diabetes diagnosis was in Germany or Austria (7.6 vs 4.9%, $P=0.52$), whereas no difference was observed for refugees from the ME (8.6 vs 8.4%, $P=0.96$).

Discussion

This is the first report on pediatric refugees from Africa or the ME diagnosed with diabetes, describing the first year of diabetes care after arrival in Germany or Austria, and based on a large well-established diabetes registry. Compared to native type 1 diabetes patients, significant differences in metabolic control, diabetes treatment and outcome among refugees from Africa or the ME were observed. This may suggest an increased need for intensified, culture-sensitive diabetes care in this particular vulnerable group of patients.

Despite overall higher costs for the health care system due to inadequate access to health care (9), previous articles still criticize restrictions for asylum seekers in Germany (10, 11, 12). Insufficient knowledge of caregivers on the grant of health care services limits refugees' access to health care (12). On the other hand, language barriers, different health beliefs, limited transport and mobility to specialized clinics and unawareness of national health system procedures may also challenge adequate diabetes care for refugee children. In the Netherlands, frequent relocations, unknown medical history and cultural differences were

reported by pediatricians as the most frequent barriers for delivering health care (13). Recently, low diabetes literacy and suboptimal diabetes disease control among Somali patients in a US primary care setting have been reported (14). Altogether, may contribute to the worse diabetes control and higher rates of severe hypoglycemia or hypoglycemia with coma in pediatric type 1 diabetes refugees from Africa or ME, compared to native children, as observed in our study. A large number of studies previously reported an association between migration and poor health care outcomes (5, 6, 15, 16) and mentioned different self-care behavior and an overall lower adherence to treatment regimen compared to the native population as potential reasons (5, 17). Life style and eating habits often differ between refugees and the host population and further challenge diabetes care for the patient and the caregiver. Apart from that, as reported by Bergenstal *et al.*, 'racial' differences in the glycation of hemoglobin partially explains HbA1c differences between African Americans and whites (18). Although clear evidence is lacking, non-glycemic hemoglobin-related factors such as red blood cell turnover are also speculated to explain ethnic differences in HbA1c (19).

In developed countries, CSII is frequently used among children and adolescents with type 1 diabetes (20). Data on CSII use in Africa or the ME are lacking. In our study, we observed a markedly lower use of modern diabetes technology such as insulin pumps in refugee children from Africa or the ME. As hypothesized by us for other migrant groups from Turkey, Southern Europe or Eastern Europe (4, 5), the lower use might be due to the high costs, lack of health care insurance and the complexity and the necessity of intensive diabetes education. Other possible contributors could be different therapeutic concepts in the home country and a potentially lower rate of acceptance of new techniques or insufficient knowledge about health care offers (4, 5). Moreover, clinicians' individual assessment whether the patient will manage a complex diabetes regimen may play a role. The uncertain procedure for granting the right of asylum may further complicate CSII initiation or other long-standing therapy decisions in newly arrived refugees.

Besides acute diabetes complications, we also observed long-term complications such as microalbuminuria or diabetic retinopathy that were more prevalent in refugees from Africa or ME compared to native children. A worse metabolic control prior to migration and an

inadequate diabetes care in the home country might be possible explanations. Apart from that, there is increasing evidence of a variety of polymorphisms that differ between populations and influence susceptibility to both, retinopathy and nephropathy (21).

Major strengths of our study are the relatively large number of pediatric diabetes cases among refugees from Africa and the ME, and the availability of data from a standardized diabetes patient registry. The registry comprises pre-defined demographic and clinical diabetes-specific parameters that are not specifically adapted to the current situation of diabetes care in refugees. Nevertheless, some weaknesses should be kept in mind. A considerable number of pediatric refugees with diabetes might be missed due to limited/unknown access to specialized diabetes clinics or undiagnosed diabetes. Additional, potentially important individual-level variables such as mental illnesses or diabetes distress that might explain disparities among refugees and the host population were not available. A cross-sectional German pilot study found a high prevalence of mental illnesses (13.7%) among unaccompanied asylum-seeking adolescents (22). Depressive symptoms and diabetes distress were reported to be higher in ethnic minorities from Turkey or Morocco compared to native type 1 diabetes patients in the Netherlands (23). Furthermore, unaccompanied children often live in nursing homes that cannot provide adequate support for the diabetes management (24). As our data do not include the family situation we are not able to differentiate this particular group. Lastly, underestimation due to under-reporting of for example hypoglycemic events might bias our findings.

In summary, our report indicates that a relevant number of pediatric refugees from Africa and the ME with type 1 diabetes are treated in German/Austrian specialized diabetes clinics. Compared to native patients, diabetes care and outcome of these children is currently suboptimal. Pediatric refugees, their parents and pediatric diabetes teams are faced with several challenges. The study may suggest the need for additional adaptations in the health care system and clinical practice to target this particularly vulnerable population in order to improve diabetes control and to prevent diabetes complications in the future.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this study.

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Author contribution statement

N P and K K wrote the manuscript, edited the manuscript, substantial contribution to conception and design and interpretation of data; C B, E H, A H, A I, J G-H, N J, C K, K M, O R, C S-S and M W researched data, contributed to discussion, reviewed and edited manuscript; R W H conceptualized the study, contributed to discussion, reviewed and edited the manuscript and is the principal investigator of the DPV initiative and as such has full access to the data. All authors approved the final version to be published.

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