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# Immigration and screening programs for hemoglobinopathies in Italy, Spain and Turkey

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**Abstract.** Sickle cell disease (SCD) and thalassemias are the most common monogenic diseases in the world. The number of migrants and refugees in Europe and Turkey, in the past decade, has increased dramatically due to war, violence or prosecutions in their homeland. Prevention and management of haemoglobin disorders is well established and managed in countries where these conditions were traditionally endemic or in countries that have a longstanding tradition of receiving migrants. Therefore, preventive and diagnostic programmes regarding hemoglobinopathies in immigrant populations have been implemented. The purpose of this paper it to report a summary of the experience gained in Italy, Spain and Turkey in migrants, asylum seekers and refugees. (www.actabiomedica.it)

**Key words:** Hemoglobinopathies, migrants, refugees, Turkey, Spain, Italy, Equality Plus Project

## Introduction

More than 270 million people worldwide are carriers of a clinically relevant hemoglobinopathy. One percent of pregnancies are at risk for disease, resulting each year in 330, 000 affected births due to sickle cell disease (SCD; 83%) or thalassemia (17%) (1).

Inherited hematologic disorders are common among many immigrant and refugee populations and should be considered in any subject who has anemia detected on screening, even if other potential causes exist. These disorders include thalassemias, SCD, enzyme defects, and cell membrane defects (2,3).

Perhaps the most widely known of these conditions is SCD, due to replacement of glutamic acid by a valine at the sixth amino acid position of the beta chain. Globally, 80% of people affected by SCD live in or have origins in central Africa. The condition also affects people from Central and South America, the Arabian Peninsula, Middle East, India, and eastern Mediterranean (4).

The thalassemias are caused by decreased or absent production of otherwise normal a- or β-globin chains. β-thalassemia major occurs in individuals who are either homozygous or compound heterozygous for a β -thalassemia mutation. The phenotype of β -thalassemia major can also result from coinheritance of β -thalassemia mutation with Hb E (Hb E/ β -thalassemia) or with a large

deletion in the β -globin gene locus (δβ -thalassemia) or in conjunction with a-globin gene duplication (5).

Historically, the prevalence of β-thalassemia has been highest in the Mediterranean region, the Middle

East, and Southeast Asia and lowest in Northern Europe and North America (4). Due to migration patterns, β-thalassemia is increasingly more common in non-endemic regions, including Western Europe and North America (6).

Screening programmes in the EU are determined at national level, and therefore there are wide variations and disparities in practice between countries. The main objective of screening for hemoglobinopathies is to improve outcomes for patients by detecting the disease early and allowing early intervention, and to allows the possibility of offering genetic counselling to parents of affected children (7,8).

The purpose of this paper it to report a summary of the experience gained in Italy, Spain and Turkey in migrants, asylum seekers and refugees.

## Italy

Around 5.1 million foreign citizens legally reside in the country (Table 1). The first ten nationalities of immigrated people, as of 1st of January 2018, living in Italy are reported in Table 2 (9).

The majority are economic migrants and their effects in terms of genetic disease, are difficult to estimate in terms of numbers with accuracy, since many factors need to be considered. Such factors include the permanency of the migration, whether it is a migration of single people or of families, whether the migrant will marry locally or from the country of origin, whether consanguineous marriage will still be practiced in the host country, whether there will be free choice partner or an arranged marriage, whether birth rate of immigrant families will be that of the home or the host country and whether there is a second generation of migrants and the customs that they have adopted (10).

### *The Italian screening programs for hemoglobinopathies and their prevalence in immigrants*

Hemoglobinopathies are not strictly a 'disease of migrants' in Italy; an extensive national population surveys for β-thalassemia begun in Italy in 1948 by Silvestroni Bianco. The Researches showed that β-thalassemia was a social problem with about 2,500,000 heterozygous individuals and over 10,000 homozygous patients (11).

The highest frequency of SCD has historically been reported in Sicily. Chromosomal analysis suggested that SCD originated from Northern Africa (12,13).

In 1998, a questionnaire, requesting information about the cases of SCD was sent to all Italian centers of

**Table 1.** Estimates of different categories of foreign population in Italy in 2017.

| | |
|---|---|
| Foreign residents (Istat 2018a) | 5,144,440 |
| Holder of a permit to stay (Istat 2018c) | 5,359,000 |
| Non-EU residence permit holders (Istat 2018c) | 3,714,137 |
| Refugees and people in fefugee-like situation (UNHCR 2018) | 167,335 |
| Migrants with no legal status (estimate) (ISMU 2018) | 490,000 |
| Asylum seekers lodging a claim in 2017 (Ministry of Interior 2018) | 126,500 |
| Total pending claims in 2017 (UNHCR 2018) | 186,648 |
| Total foreign population (Eurostat estimate 2018) | 6,053,960 |
| Number of immigrants naturalised in the last 10 years (Istat 2018c) | 1,081,000 |

*(Source: Caritas Italiana. Common home migration and development in Italy. May 2019.pp.1-30; by courtesy of Scripta Manent, Milan- Rivista Italiana di Medicina dell'Adolescenza -2020)*

**Table 2.** First 10 nationalities of immigrated people, as of 1st of January 2018, living in Italy.

| Nationality | Total | Females | Males |
|---|---|---|---|
| Romania | 1,190,091 | 684,130 | 505,961 |
| Albania | 440,465 | 215,362 | 225,103 |
| Morocco | 416,531 | 194,599 | 221,932 |
| China | 290,681 | 144,231 | 146,450 |
| Ukraine | 237,047 | 184,780 | 52,267 |
| Philippines | 167,859 | 95,260 | 72,599 |
| India | 151,791 | 62,042 | 89,749 |
| Bangladesh | 131,967 | 35,543 | 96,424 |
| Moldova | 131,814 | 87,505 | 44,309 |
| Egypt | 119,513 | 39,119 | 80,394 |

*(Source: Caritas and Migrantes 2017/2018. Elaboration on ISTAT data; by courtesy of Scripta Manent, Milan- Rivista Italiana di Medicina dell'Adolescenza -2020)*

Pediatrics and determined the distribution and severity of SCD in Italy. A total of 696 cases were reported. The distribution of registered patients showed that, although the S gene originated mostly in Sicily, with an estimated mean frequency of 2% and a peak of 13%, and Southern Italy, 20% of patients with SCD lived in Central and Northern Italy (14).

According to 2019 data from the National Registry of Thalassemia and Haemoglobinopathies, in Italy there are approximately 1,275 patients living with SCD. The epidemiology of SCD has changed considerably in the country over recent years, in particular in response to changes in migratory patterns and migration from countries with high SCD prevalence (13).

Therefore, implementation of screening programs for early detection of patients with SCD has become necessary in Italy as a result of the high rate of migration from areas with a high prevalence of the disease (Sub-Saharan Africa, Middle East and the Balkans).

A screening programs for early detection of patients with SCD was conducted from 2014 to 2016. Samples from 17,077 new mothers were analyzed and 993 showed alteration of Hb patterns (5.8%) (1.0% Hb AS carriers); of the 1011 at-risk newborns, four (0.4%) carried SCD and 90 (8.9%) were Hb AS carriers. The Authors also detected 268 (32.1 %) β-thalassemia heterozygous, 24 (2.9 %) δ thalassemia heterozygous, 6 (0.72 %) persistent HbF or δ/β thalassemia heterozygous. Altered levels of HbA2 and HbF were also reported: 103 women (12.35 %) showed decreased values of HbA2 (<2%), 32 (3.83 %) were identified to be carrier of HbA2 borderline (3.2-3.8%) and 156 (18.70 %) had increased HbF levels. These data provided valuable information on the frequency of these conditions in geographic areas in which the disease was historically rare (15).

The experience on new cases of SCD and other hemoglobinopathies in refugees, between 2014 and 2017, at 13 Italian reference centers for hemoglobinopathies was reported by De Franceschi et al. (16). A total of 70 patients with hemoglobin disorders were identified (61 new patients with SCD, 6 with transfusion- dependent thalassemia, and 3 with other hemoglobinopathies), the majority of whom were male. Half were adults with the median age of 21 years and the other half were children. Most came from West African countries Senegal and Nigeria, as well as Morocco, Egypt, and Tunisia in North Africa, and Syria in the Middle East. Approximately two-thirds of the 70 patients were diagnosed after an acute complication requiring emergency care and some of these complications, likely preventable with early diagnosis and treatment, were life-threatening (16). To expedite the identification of SCD and mitigate complications, the same Researcher (17) undertook a pilot study in which they performed point-of-care screening of refugees seen in a single refugee center during October 2017. Three percent were found to have SCD and 20% were found to have the heterozygous AS genotype. The majority of sickle hemoglobin (HbS) carriers were from West Africa, and the authors noted that "none of the newly identified SCD patients were aware of their condition ". These findings prompted the researchers (17) to propose several initiatives to improve screening of SCD among migrants arriving to Italy, in particular:

- Routine screening for SCD in refugees from countries endemic for SCD within 10-14 days from their arrival to identify potentially vulnerable patients
- A structured, collaborative national network
- Educating ED physicians to identify and treat acute SCD-related events ( such as: SCD-related acute vaso-occlusive events)
- Rapid referrals of refugees with SCD or symptomatic HbS-carrier genotype to a comprehensive SCD reference center.
- Earlier initiation of disease-modifying treatment (e.g., hydroxyurea).

Together, these data suggest that the increased number of patients with SCD in Italy has mostly resulted from migratory patterns of immigrants arriving, in recent years, from countries in which there is a high disease prevalence (13). Comprehensive prevention programs including public education, genetic counseling, and population screening, accompanied by prenatal diagnostics are recommended. It is generally recognized that registries are important tools for detecting demographic patterns, allocating resources, monitoring patient outcomes, and guiding decisions (18,19). The main challenges for physicians were lack of awareness of the asylum seekers' specific health care problems,

language and intercultural communication problems, as well as access and integration of asylum seekers into the health care system, Language barriers and poor multicultural competencies should be also considered (16,17).

**Spain**

As in other Mediterranean countries, the main hemoglobin disorder in Spain is β-thalassemia. Until 2003, however, the prevalence of hemoglobinopathies in Spain was unknown, and only the establishment of universal pilot screening programs of hemoglobinopathies allowed to identify an overall incidence of 0.33% (20,21).

The first study of hemoglobinopathies in Spain was carried out in 1981, in Barcelona by Baiget et al. (22). The Authors reported a global prevalence of hemoglobinopathies of 0.14%, a value significantly lower value than that reported by the WHO in 1995 (23).

Although after this first publication, many studies have been carried out to establish the prevalence of β-thalassemia in Spain, in only one, the individuals included were representative of almost all Spanish geographical regions (24). This study demonstrated that β-thalassemia distribution was very heterogeneous with a prevalence ranging from 0.1% to 5% and pointed out that most of the HbS, and also HbC and other hemoglobinopathies carriers, were from southern and western geographical regions of Spain. Moreover, control programs based on the screening of couples at risk for thalassemia and the offer of antenatal diagnosis resulted beneficial for reducing the frequency of β-thalassemia major (25). Noteworthy, some of the Spanish regions exhibited a significantly higher prevalence of both b- thalassemias and structural hemoglobinopathies, most probably due to the well known genetic influence of Arab populations in the past (26).

Between 2003 and 2008, a pilot study for neonatal screening of hemoglobinopathies was performed in Catalonia by Man˜ú et al. (27,28) with the support of a grant of the Spanish Ministry of Health.

A total of 4696 newborns from at-risk ethnic groups were studied using two different targeted neonatal screening approaches. Neonates were classified into four different categories according to mother's birthplace: 1) North Africa; 2) Sub-Saharan Africa; 3) Asia, and 4) Central and South America. The prevalence of hemoglobinopathies and SCD was calculated for each category and are illustrated in table 3.

After 2003, the increasing immigration flows, especially from Africa (Northern and Sub-Saharan regions) led to the emergence of SCD as one of the most common hereditary disorders in Spain, with an impact on the burden of healthcare in several of its geographical regions. In these regions,

the prevalence of SCD was directly related to the impact of immigrant populations, mainly from sub-Saharan Africa (29). The national consensus in Spain indicated that the number of African immigrants has doubled in only 5 years. Furthermore, the distribution of this immigrant African population was very heterogeneous and differed widely from one region to another (Table 4)

In conclusion, all the studies performed until 2008, demonstrated that in Spain the prevalence of hemoglobinopathies was lower when compared to other Mediterranean countries (30) or concerning the European median (0.5 cases for thalassemia and 15 for SCD per 100,000 inhabitants) (31). Moreover, the prevalence of SCD was heterogeneous and strongly influenced by the migratory flows.

After 2008, the most updated information on the current situation of hemoglobinopathies in Spain has been recently published by the Spanish Society of Pediatric Hematology and Oncology (SEHOP) from a multicentric study with the participation of 51 hospitals all over Spain in which 75 thalassemias (62 thalassemia major), 826 SCD and 58 other hemoglobinopathies were registered (Table 5) (32).

A national registry of hemoglobinopathies was implemented in 2014. Fifty hospitals participated to the survey. Thalassemia was reported in 73 cases and SCD in 615 cases. The incidence in 2014 was estimated at 4 cases of thalassemias and 14 cases of SCD among 426.303 live births (0.002 per 1.000 live births and 0.03 per 1.000 live births, respectively) (33).

In summary, the current influx of economic migrants and asylum seekers in Spain, from countries with a high prevalence of haemoglobinopathies, creates new challenges for health care systems and

**Table 3.** Number of births from African origin immigrants (and indigenous residents of African ethnicity) and estimation of SCD prevalence in different Spanish regions (2006) *( by courtesy of Scripta Manent, Milan- Rivista Italiana di Medicina dell'Adolescenza -2020).*

| Region | No. of births | Africa (%) | North Africa (%) | Sub-Saharan (%) | N° cases of SCD (prevalence in %) |
|---|---|---|---|---|---|
| Andalusia | 95 304 | 2400 (2.5) | 2085 (2.1) | 315 (0.33) | 4.8 (0.005) |
| Aragòn | 12 280 | 807 (6.5) | 518 (4.2) | 289 (2.35) | 3.7 (0.030) |
| Asturias | 7596 | 51 (0.6) | 51 (0.6) | 16 (0.21) | 0.2 (0.003) |
| The Balearic Islands | 11 675 | 828 (7.0) | 631 (5.4) | 197 (1.69) | 2.6 (0.023) |
| The Canary Islands | 20 668 | 617 (2.9) | 400 (1.9) | 217 (1.05) | 2.8 (0.013) |
| Cantabria | 5229 | 35 (0.6) | 22 (0.4) | 13 (0.25) | 0.2 (0.003) |
| Castilla y Leòn | 19 775 | 441 (2.2) | 405 (2.0) | 36 (0.18) | 0.6 (0.003) |
| Castilla-La Mancha | 20 389 | 699 (3.4) | 649 (3.1) | 50 (0.25) | 0.9 (0.004) |
| Catalonia | 82 300 | 7207 (8.7) | 5986 (7.2) | 1221 (1.48) | 17.4 (0.021) |
| Valencia | 52 756 | 2453 (4.6) | 2036 (3.8) | 417 (0.79) | 5.9 (0.011) |
| Extremadura | 10 118 | 203 (2.01) | 199 (1.9) | 4 (0.04) | 0.1 (0.001) |
| Galicia | 21 392 | 161 (0.75) | 115 (0.5) | 46 (0.22) | 0.6 (0.003) |
| Madrid | 71 912 | 2690 (3.7) | 1888 (2.6) | 802 (1.12) | 10.4 (0.014) |
| Murcia | 18 091 | 1443 (7.9) | 1358 (7.5) | 85 (0.47) | 1.7 (0.009) |
| Navarra | 6551 | 384 (5.8) | 310 (4.7) | 74 (1.13) | 1.0 (0.016) |
| Basque Country | 20 026 | 388 (1.9) | 259 (1.2) | 129 (0.64) | 1.7 (0.008) |
| La Rioja | 3070 | 289 (9.4) | 254 (8.2) | 35 (1.14) | 0.5 (0.018) |
| Ceuta | 1041 | 140 (13.4) | 138 (13.2) | 2 (0.19) | 0.1 (0.009) |
| Melilla | 1122 | 383 (34.1) | 372 (33.1) | 11 (0.98) | 0.3 (0.027) |

diagnostic laboratories. The incidence of hemoglobinopathy is lower in Spain than in other Mediterranean countries, with a prevalence of approximately 1.5 cases per 100.000 people. Pediatricians and pediatric societies should work to improve the sensitivity of their respective populations towards migrants, asylum seekers, and refugees.

**Turkey**

Turkey is located in the intersection point of Asia, Europe and Africa and Turkey is a bridge between economically and politically underdeveloped states and rich Western countries.

Turkey is at the centre of refugee movements due to historical and geographical reasons. Turkey did not have a specific refugee policy until the 1950s and did

**Table 4.** Distribution of African immigrants and indigenous residents of African ethnicity in the different regions of Spain (2008) (by courtesy of Scripta Manent, Milan- Rivista Italiana di Medicina dell'Adolescenza -2020).

| Region | Total population | Africa countries (%) | North Africa (%) | Sub-Saharan (%) |
|---|---|---|---|---|
| Andalusia | 8 177 805 | 120 295 (1.47) | 98 298 (1.20) | 21 997 (0.27) |
| Aragòn | 1 325 272 | 31 282 (2.36) | 19 699 (1.49) | 11 583 (0.87) |
| Asturias | 1 079 215 | 3738 (0.35) | 2022 (0.19) | 1716 (0.16) |
| The Balearic Islands | 1 071 221 | 30 027 (2.80) | 21 634 (2.02) | 8393 (0.78) |
| The Canary Islands | 2 070 465 | 27 804 (1.34) | 16 733 (0.81) | 11 071 (0.53) |
| Cantabria | 581 215 | 2523 (0.43) | 1526 (0.26) | 997 (0.17) |
| Castilla y Leòn | 2 553 301 | 20 919 (0.82) | 18 068 (0.71) | 2851 (0.11) |
| Castilla-La Mancha | 2 038 956 | 34 209 (1.68) | 30 188 (1.48) | 4021 (0.20) |
| Catalonia | 7 354 441 | 275 746 (3.75) | 216 180 (2.94) | 59 566 (0.81) |
| Valencia | 5 016 348 | 102 377 (2.04) | 82 366 (1.64) | 20 011 (0.40) |
| Extremadura | 1 095 894 | 9847 (0.90) | 9378 (0.86) | 469 (0.40) |
| Galicia | 2 783 100 | 8549 (0.31) | 5146 (0.18) | 3403 (0.12) |
| Madrid | 6 251 876 | 112 860 (1.81) | 78 817 (1.26) | 34 043 (0.54) |
| Murcia | 1 424 063 | 67 863 (4.77) | 60 818 (4.27) | 7045 (0.49) |
| Navarra | 619 114 | 12 984 (2.10) | 10 069 (1.63) | 2915 (0.47) |
| Basque Country | 2 155 546 | 20 089 (0.93) | 13 344 (0.62) | 6745 (0.31) |
| La Rioja | 3 17 020 | 9532 (3.01) | 8096 (2.55) | 1436 (0.45) |
| Ceuta* | 77 320 | 2620 (3.39) | 2610 (3.38) | 10 (0.01) |
| Melilla* | 71 339 | 5225 (7.32) | 5215 (7.31) | 10 (0.01) |

** Regions in the north of the African continent.*

not have a strategy for the social inclusion of migrants and therefore was not ready for the recent high influx of migration. The first policies to be implemented regarding migration and refugees came with the establishment of United Nations Turkey signed the 1951 convention and its 1967 protocol with a geographical restriction. In April 2014, the Law on Foreigners and International Protection (LFIP) established a proactive migration

**Table 5.** Characteristics of the registered 959 patients with hemoglobinopathy in Spain (Medicina Clinica. 2020; 155:95-103; by courtesy of Scripta Manent, Milan- Rivista Italiana di Medicina dell'Adolescenza -2020)

| | Thalasemia | Sickle Cell Disease (SCD) | Other Hemoglobinopathies | Total |
|---|---|---|---|---|
| Number of patients (%) | 75 (7.8) | 826 (86.1) | 58 | 959 (100) |
| | Major 62 (6.5)<br>Minor 13 (1.3) | SS: 653 (68.1)<br>SC: 100 (10.4) | HbH: 12 (1.2)<br>HbCC: 8 (0.8) | |
| | | $S^{+}$: 34 (3.5) | Other: 38 (4.0) | |
| | | $S^{0}$: 33 (3.4) | | |
| | | $S^{0}$: 33 (3.4) | | |
| | | Unknown: 6 (0.6) | | |
| Male/Female ratio | 0.94 | 1.11 | 0.79 | 1.04 |
| Alive (%) | 43 (69.3) | 521 (63.1) | 40 | 604 (63.8) |
| Dead (%) | 2 (3.2) | 18 (2.2) | 2 | 22 (2.3) |
| Failed follow-up (%) | 17 (27.4) | 286 (34.6) | 17 | 320 (33.8) |
| Age at diagnosis (years) | 0.7 (0-3.8) | 2.7 (0-52.0) | | |
| Current age (years) | 10.9 (0.7-64.3) | 10.2 (0.7-55.7) | | |
| Time of follow-up (years) | 11.0 (2.2-44.7) | 8.4 (0-33.5) | | |

policy to cope with migration influxes, without infringing fundamental human rights of asylum seekers (34).

Since the beginning of the Syrian civil war, started in March 2011, millions of refugees immigrated mostly to neighbouring countries. According to the Turkish report of Health Services on Temporary Protection of General Directory of Public Health of MOH, in 2019 approximately 3.6 million of immigrants were under temporary protection (35).

Turkey has also been receiving migrants form some African countries, such as Eritrea, Somalia, Egypt and Sudan. These migrants usually consider Turkey not as the final destination of their travel, but rather a transit country. The official total number of irregular migrants who passed through Turkey to Europe between 2009 and 2013 was 225,590 (36).

Irregular migrants consider Turkey as a transit route. In addition, Turkey has rising power in its region and this makes Turkey a destination country instead of transit country for third country nationals. Besides, the turmoil which has continued for years in the Middle East, Caucasus and the Balkans has led to a mass influx to Turkey and Turkey has welcomed asylum seekers in a difficult situation as a consequence of its historical ties and its sense of obligation. After 1980s, Turkey has become not only immigrant sending country but also immigrant receiving country. Conflict, violence and persecution worldwide force due to the number of people displaced by Turkey reached record levels, the highest number in the world continues to host refugees.

Turkey already serves to host 3.4 million registered Syrian refugees and about 370.000 people from other nations (37). In Turkey, an estimated 3.4 million Syrian refugees have entered the country since 2011, with 276. 158 babies being born to Syrian couples living in Turkey between 2011 and 2017 (38). These couples were not covered by the premarital screening program that was widely implemented in Turkey in 2002. In 18 pediatric hematology/ oncology centers throughout Turkey, 318 children from 235 refugee families had β-thalassemia (mean age 8.1 years); most of these patients presented with an inadequate transfusion and chelation history. A total of 72 of 318 affected children from refugee families were born in Turkey,

**Table 6.** Foreign Nationals Polyclinics (YUP) data for immigration in Turkey (From: www.goc.gov.tr. Directorate General of Migration Management of Ministry of Interior of Republic of Turkey; by courtesy of Scripta Manent, Milan- Rivista Italiana di Medicina dell'Adolescenza -2020).

| Number | Total 2018 | Total 2019 | Total |
|---|---|---|---|
| Application | 65.416 | 93.079 | 158.855 |
| Examination | 49.525 | 72.934 | 122.459 |
| Vaccine | 44.464 | 53.225 | 97.689 |
| Following up baby | 5.759 | 7.263 | 13.022 |
| Following up children | 1.904 | 3.410 | 5.314 |
| Following up pregnant | 1.480 | 1.995 | 3.475 |

indicating an urgent plan to screen refugee couples at risk for hemoglobinopathies (39).

In order to provide preventive health services and basic health services to Syrians in our country more effectively and efficiently, to overcome the problems arising from the language and cultural barrier, and to increase access to health services, the immigrant health centers (GSM) are established.

Currently, 780 migrant health units have been established in 180 migrant health centers in 29 provinces and continue their activities.

"Syrians Temporary Protected Health Status and Development of the Republic of Turkey presented by Related Services Project (Feelings)" framework; Efforts are being made to support the currently operating GSM's, to create new GSM where needed, and to employ Syrian health workers to provide services in these centers. The number of Syrian physicians employed in GSM is 694, the number of Syrian auxiliary health personnel is 954, the number of patient referral personnel is 1,121, the number of support services personnel is 399, the number of social workers is 11 and the number of psychologists is 12.

Increasing the service capacity for migration health by training TSM personnel working in these centers on migration and migrant health is among the goals (40) (Table 6).

Hemoglobinopathies are a very important health problem in Turkey. In 1958, the first clinical and hematological studies were published by Aksoy et al. In 1971, Cavdar and Arcasoy reported that the overall incidence of β-thalassemia was 2.1% (41,42).

Altay published abnormal hemoglobins in Turkey in different years. Forthy-two abnormal hemoglobins were identified in the Turkish population. The most frequently observed abnormal hemoglobins were: Hb S, Hb D, Hb C, HbE and Hb O Arab. HbS was the most common abnormal hemoglobin in Turkey (43).

The Ministry of Health (MOH) established thalassemia centers in Antalya, Antakya, Mersin and Mugla, the southern provinces of Turkey, after the law named "Fight Against Hereditary Blood Disease (FAHBD") was accepted in 1993.The Turkish National Hemoglobinopathy Council (TNHC) was installed to combine all centers, foundations and associations into one organization together with the MOH in 2000. The written regulations of FAHBD were published in 2002.Thirty-three provinces situated in the Thrace, Marmara, Aegean, Mediterranean and South Eastern regions were selected for the Hemoglobinopathy Prevention Program. (HPP) by MOH and TNHC. A premarital hemoglobinopathy test is mandatory and free of charge in this program. The number of newborn with thalassemia and hemoglobinopathies were 272 in 2002 and dropped to 25 in 2013. There has been a 90.0% reduction in affected newborns as the results of educational and prevention in the last 10 years. This program has been run as successfully in 41 provinces by the MOH till to 2013.(44,45)

As of November 1, 2018, the hemoglobinopathy Control Program has been implemented in 81 provinces covering whole country, under the name of "Pre-Marriage Hemoglobinopathy Screening Program" (46).

Mediterranean Blood Diseases Foundation (AKHAV), the European Network for Rare and Congenital Anaemias (ENERCA) and the International Network of Clinicians for Endocrinopathies in Thalassemia and Adolescence Medicine (ICET-A) through the Equality Plus project of the EU have planned a common response to the rising number of SCD patients in Italy, Spain and Turkey with the objectives to create a national working group focused on subjects with hemoglobinopathies and to develop tailored guidelines and algorithms for the management of SCD that could be accessed and practiced by those involved in the care of these patients in order to improve their specific knowledge and their ability of communication with different cultures and to deal with the medical needs of patients with hemoglobinopathies, considering the insufficient level of knowledge of medical teams who are now having to take care of these patients.

## Conclusion

Through mobility and migration flows, haemoglobinopathies have spread from the Mediterranean, Africa and Asia to the whole Europe, the Americas and Australia, and there is scientific evidence that they have become a global public health problem. Prevention and management of haemoglobin disorders is well established and managed in countries where these conditions were traditionally endemic or in countries that have a longstanding tradition of receiving migrants. Preventive strategies of the public health authorities that today are lacking, should be include three different types of actions: a) information for foreign populations and caregivers; b) healthy carriers detection among immigrants (screening programs); and c) counselling and prenatal diagnosis for healthy carriers and at-risk immigrant couples (47).

Many questions remain unanswered due to the lack of standardized national data collection systems across Europe. Coordinated efforts should be made to develop diagnostic pathways for hemoglobinopathies, in order to plan interventions, including prenatal diagnosis and cure. The absence of national registries makes essential to identify ways and tools to better describe the extent of the problem in terms of numbers and distribution across each country (48,49).

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