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MINI REVIEW

Thalassemias and Hemoglobinopathies in Turkey

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Abstract

Thalassemias and hemoglobinopathies are a serious health problem in Turkey. There is a 70-year history of thalassemia in Turkey. The first patient with β-thalassemia major (β-TM) was reported in 1941. The first clinical and hematological studies were published by Aksoy in 1958. The overall incidence of β-thalassemia (β-thal) was reported by Çavdar and Arcasoy to be 2.1% in 1971. Important steps such as written regulations, education and prevention campaigns, have been taken to prevent thalassemia in Turkey by the Ministry of Health (MOH), the Turkish National Hemoglobinopathy Council (TNHC) and the Thalassemia Federation of Turkey (TFT) since 2000. A national hemoglobinopathy prevention program was started in provinces with a high prevalence by the MOH in 2003. While the percentage of premarital screening test was 30.0% of all couples in 2003, it reached 86.0% in 2013. While the number of newborn with thalassemias and hemoglobinopathies was 272 in 2002, it had dropped to 25 in 2010. There has been a 90.0% reduction of affected births in the last 10 years.

Keywords

Education, hemoglobinopathies, premarital screening, prevention, thalassemia, Turkey

History

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Introduction

Thalassemias and hemoglobinopathies are a serious health problem wordwide. It is estimated that in excess of 300,000 children are born each year with a severe inherited disorder of hemoglobin (Hb) (1). There is a 70-year history of thalassemia in Turkey. Some important milestones of thalassemia in Turkey follow: the first patient with β-thalassemia major (β-TM) was reported in 1941 (2). In 1958, the first clinical and hematological studies were published by Aksoy *et al.* (3). In 1971, Çavdar and Arcasoy reported that the overall incidence of β-thalassemia (β-thal) was 2.1% (4). In 1983, the first prenatal diagnostic procedures for identifying hemoglobinopathies were performed by Beksac *et al.* (5). In 1987, Akar *et al.* (6) showed that the most frequent thalassemia allele in the Turkish population was the IVS-I-110 (G > A; *HBB*: c.93-21G > A) mutation, being the most common thalassemia mutation in the majority of the high risk regions of the Mediterranean area. Canatan and Arcasoy (7) published that the first stem cell transplantation was performed by Ozerkan in a patient with thalassemia. In 1992, Başak *et al.* (8) reported the spectrum of β-thal mutations occurring in the Turkish population. The six most frequent alleles were: IVS-I-110, IVS-I-6 (T > C; *HBB*: c.92 + 6T > C), frameshift codon (FSC) 8 (–AA; *HBB*: c.25_26delAA), IVS-I-1 (G > A; *HBB*: c.92 + 1G > A), −30 (T > A; *HBB*: c.-80T > A) and FSC 5 (–CT; *HBB*: c.17_18delCT) account for only 70.0% of the mutations. In 2002, Altay (9) published screening studies for abnormal Hbs and β-thal during the last 40 years. These studies revealed the most common abnormal mutation was Hb S (*HBB*: c.20A > T) followed by Hb D-Punjab (*HBB*: c.364G > C), Hb E (*HBB*: c.79G > A) and Hb O-Arab (*HBB*: c.364G > A). In addition, another 42 abnormal Hbs were identified in the Turkish population (9). In 2004, Kahraman *et al.* (10) performed preimplantation genetic diagnosis for thalassemia combined with HLA typing in Turkey. The aim of this study was to emphasize the studies of education and prevention on the thalassemias and hemoglobinopathies in Turkey.

Materials and methods

The Ministry of Health (MOH) planned to establish 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 first thalassemia center was established at the Antalya State Hospital, Antalya, Turkey by Canatan *et al.* (11) in 1994. The Turkish National Hemoglobinopathy Council (TNHC) was installed to combine all centers, foundations and associations into one organization together with the MOH in 2000 (12). The Thalassemia Federation of Turkey (TFT) joined all the associations as a secular society organization instead of TNHC in 2005.

Hemoglobinopathy prevention program

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

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(HPP) by MOH and TNHC. The HPP was started in these provinces on May 8 2003. The HPP had the following goals: (1) to assess the present situation of thalassemias and hemoglobinopathies in Turkey, (2) to establish first level centers for prevention programs, (3) to educate the healthcare personnel about thalassemia, (4) to inform the community by using press and media, (5) to provide premarital screening tests and genetic counseling to couples. According to the written regulations, first level centers were responsible for diagnosis, public education, screening and genetic counseling. Second level centers were responsible for the diagnosis, therapy and follow-up of patients. Third level centers were for prenatal diagnosis, genetic analysis or stem cell transplantation.

Educational studies

The National Thalassemia Prevention Campaign (NTPC) and Teacher Education Program (TEP) were organized for public education to support HPP by the MOH and TFT in 2007. A total of 63,000 persons such as health workers, students, teachers, managers of villages or demarchs, religion officers and many other people were informed about thalassemias and the hemoglobinopathies (13).

A total of 3600 health personnel were educated on thalassemia prevention and therapy by National Thalassemia Education Seminars (NTES) in 2009 and 2010. A total of 3000 patients and parents with thalassemia have been educated by six international thalassemia summer schools (ITSS) since 2000. A total of 2000 thalassemic patients have been educated by 10 National Thalassemia Youth Camps (NTYC) since 2000.

The 12th Thalassemia International Federation (TIF) Congress was organized by MOH, TFT and TIF in Antalya in 2011. A total of 1350 persons from 60 countries participated in this congress.

Results

The status of centers

Premarital thalassemia test is mandatory and free of charge in Turkey. According to reports from the MOH, there are 36 first level hemoglobinopathy diagnostic centers for premarital tests, six second level centers for following up patients, six third level centers for prenatal diagnosis and stem cell transplantation (14,15).

The results of prevention and education

While the percentage of premarital screening tests were 30.0% of all couples in 2003, it reached 86.0% in 2013 (Figure 1). The number of newborn with thalassemia and hemoglobinopathies were 272 in 2002 and dropped to 25 in 2010. As a result, there has been a 90.0% reduction in affected births (15).

The status of the traits

The MOH and TNHC picked up the screening results from 16 different cities in the Marmara, Aegean and Mediterranean region between 1995 and 2000. A total 380,000 healthy subjects were screened in these provinces, an average frequency of 4.3% β-thal trait was found.

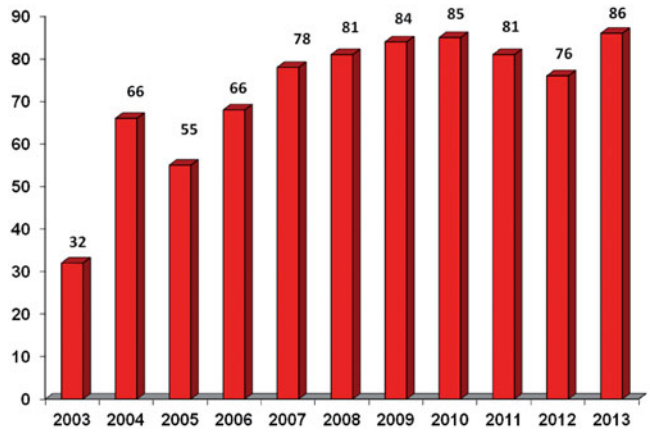

Figure 1. The percentage of premarital thalassemia tests performed in Turkey between 2003 and 2013 (15).

The highest prevalence of β-thal and Hb S trait were found in the West Mediterranean and in the East Mediterranean, with a frequency of 13.1 and 10.0%, respectively. There are about 1.5 million thalassemia and hemoglobinopathy traits according to a hemoglobinopathy control program in Turkey (12).

The status of the patients

The MOH and TNHC made an inventory of all recorded patients with thalassemia and abnormal Hbs from 81 provinces of Turkey in 2001. There were 4513 registered patients with thalassemia and abnormal Hbs. Two thousand, five hundred and seventy-three of these patients had β-TM (57.0%), 1050 had sickle cell disease (23.0%), 700 had β-TI (15.5%) and the remaining 190 patients (4.5%) had various combinations of other abnormal Hbs. The number of patients were about 5500 in 2010 (12,15). All the patients have health coverage with social security.

Status of transfusion

Erythrocyte suspensions and filtration procedures for all patients are provided free of charge by the Red Crescent blood centers or University Blood Centers. The first time, special voluntary blood donation campaign for patients with thalassemia, named Blood Mother and Blood Father, was launched by Mediterranean Blood Diseases Foundation in Antalya in 1996 (16). Then the Thalassemia Federation and the Turkish Red Crescent Society signed a protocol and the project was named ''Let the Flowers Fade Thalassemia Campaign'' at the World Thalassemia Day on May 8 2006.

Status of chelation

The chelator deferoxamine (DFO) has been used alone by patients with thalassemia since the 1980s in Turkey. The oral chelator deferiprone (L1) was licenced specifically for patients with β-TM in 2004. Another oral chelator deferasirox (DFX) was approved by the MOH for the treatment of patients with transfusional iron overload in 2008. There is no clear and sufficient data about how many patients are using which chelator or combination chelator regimen in Turkey.

Discussion

The first studies on preventing thalassemia were started in Mediterranean countries in the 1970s by the World Health Organization (WHO). The WHO guidelines for the control of Hb disorders included optimal management for patients, community-based prevention education, prospective heterozygot screening programs, genetic counseling and prenatal diagnosis services based on integrated strategy definitions (17,18).

The first screening survey of thalassemia carriers among the students started in Latium, Italy in 1975 (19). The mean percentage of cooperation was 70.0% and the mean percentage of thalassemia was 2.42%. (19).

A national program for the prevention of hemoglobinopathies in Greece was assessed during the last 30 years. Overall, the reduction in new cases were 81.1 and 84.6% for β-TM and sickle cell diseases, respectively (20).

The first epidemiological study for thalassemia in Cyprus determined that the frequency of β-thal carriers was around 18.0% (21). A program for the prevention of homozygous β-thal has been in operation in Cyprus from 1973 (22).

The first scientific studies on thalassemia started in North Cyprus in 1976. Due to the thalassemia prevention program, the number of newborn thalassemic babies dropped by one every 2-3 years between 1991 and 2001. No thalassemic babies have been born in the last 5 years (23).

The frequency of β-thal incidence is 2.0-3.0% in the population of Bulgaria (24). Haplotype I and the splicing mutation in IVS-I-110 are the most common in Bulgaria, like all Mediterranean ethnic groups (8,22,23,24).

The HbVar database of Hb variants and thalassemia mutations is one of the oldest. HbVar is based on The Human Hemoglobin Variants and Thalassemia Syllabi by Huisman, Carver, Efremov and Baysal dating from 1996 to 1998. To date there are 837 *HBB* gene entries for 28 populations and 27 ethnic groups in the HbVar database (25,26).

The first clinical and hematological studies were published by Aksoy *et al.* (3) in Turkey in 1958. Çavdar and Arcasoy (4) reported that the overall incidence of β-thal was 2.1%. The year 2000 has become a milestone in our country for the thalassemia topic. International summer schools and national youth camps were added to the scientific studies and service studies. The MOH, TNHC and TFT have made great strides in the prevention of thalassemia in the last 10 years (27).

The HPP was started in 33 provinces on May 8 2003. Newborn thalassemic patients have been reduced by 90.0% in the last 10 years (15). This program is now being successfully run in 41 provinces by the MOH in 2013.

There are about 1.5 million thalassemia trait and about 5500 patients with thalassemia and hemoglobinopathies in Turkey. There has been a 90.0% reduction in affected newborns as the results of educational and prevention studies in Turkey. All the patients are under the umbrella of social security. Transfusion and chelation regimens are supplied free of charge.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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