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Distribution of hemoglobinopathy disorders in Saudi Arabia based on data from the premarital screening and genetic counseling program, 2011–2015

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ABSTRACT

The prevalence rates of β-thalassemia (β-thal) and Sickle Cell Disease (SCD) in Saudi Arabia are considered one of the highest compared to surrounding countries in the Middle East (0.05% and 4.50%, respectively). In this study, Secondary data analysis was obtained from the premarital screening and genetic counseling program (PMSGC), and included 12,30,582 individuals from February 2011 to December 2015. Prevalence rates (per 1000 population) for β-thal and SCD were calculated for carrier status, disease status and their combination. During the 5-year study period, the overall prevalence rate per 1000 population for β-thal was 13.6 (12.9 for the trait and 0.7 for the disease). The prevalence rate for SCD was 49.6 (45.8 for the trait and 3.8 for the disease). Rates for β-thal were found to decrease from 24.2 in 2011, to 12 in 2015. However, SCD rates remained rather constant and ranged from 42.3 in 2011 to 49.8 in 2015. The highest rate for both β-thal and SCD was observed in the Eastern and Southern regions. This result reflects major accomplishment of the PMSGC. This study recommends further improvement in preventive measures in high-risk regions, and enhanced community awareness to provide the highest rate reduction for these disorders.

1. Introduction

Hemoglobinopathies, genetic disorders of hemoglobin, are the most common inherited disease in humans [1]. Global estimates indicate that approximately 3,00,000–4,00,000 infants are diagnosed yearly with hemoglobin disorders [2]. Two hemoglobinopathy disorders, thalassemia and sickle cell disease (SCD), have received significant attention of the global public health community due to their impact on increased mortality and morbidity among affected individuals [3,4]. Some forms of these disorders are considered serious autosomal recessive phenotype disorders, such as beta-thalassemia (β-thal) major, a lethal genetic disorder [5]. Yearly, approximately 240 million cases of heterozygous β-thal are diagnosed worldwide, mostly in the Mediterranean islands and in parts of Southeast Asia [6,7]. Worldwide SCD incidence in newborns was estimated to be 3,00,000 in 2008 [7]. SCD prevalence has been significantly increasing in most of sub-Saharan Africa, the Mediterranean, and the Middle East [7]. The prevalence rates of β –thalassemia (β-thal) and Sickle Cell Disease (SCD) in Saudi Arabia are considered one of the highest compared to surrounding countries in the Middle East (0.05% and 4.50%, respectively) [8].

Preventive screening programs have been adopted in several countries worldwide to reduce the prevalence of β-thal and SCD [9]. First, a premarital screening program was established in 1976 in Rome to determine the β-thal traits among students in a group of intermediate schools [10]. This was followed in 1980 by the establishment of an SCD preventive program in Virginia [1]. After this, many countries worldwide also adopted different types of preventive programs: premarital carrier screening, family-oriented approach to prevention, neonatal screening, antenatal screening for chromosome abnormalities and congenital malformations, and pre-implantation genetic diagnosis [11]. Countries that successfully implemented these programs included Italy, Greece, Cyprus, France, Iran, Thailand, Australia, Singapore,

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Taiwan, Hong Kong, and Cuba [9]. The goal of complete eradication for β-thalassemia was met in Cyprus, Italy, and Greece [12].

In the Middle East, eight countries have established premarital screening and genetic counseling programs (PMSGC), which constitute a mandatory step prior to receiving a marriage license and offer genetic counseling to couples at risk for hemoglobinopathy disorders [10]. Saudi Arabia introduced this program in 2001 and made it mandatory by 2004 [12]. A handful of studies have been conducted since 2004; they have shown a minor decline in the prevalence of SCD, but there were inconsistent reports about the prevalence of thalassemia. Six years after the launching the program, researchers have found a marked decrease in the number of at-risk marriages and have predicted a considerable reduction in the genetic disease burden in Saudi Arabia in upcoming years.

Overall, there is a great need for reducing the burden of hemoglobinopathy disorders, specifically the β-thal and SCD in Saudi Arabia. Having a successful mandatory premarital testing program will contribute to this target. Ongoing monitoring of trends in hemoglobinopathy disorders over time is necessary to evaluate the success of the PMSGC program in achieving the targeted reduction, and eventually elimination, of disease burden. In the light of this situation, this study was conducted to assess recent time trends in β-thal and SCD prevalence rates and their distribution by demographic characteristics and geographic regions in Saudi Arabia using data from the PMSGC program for the period of February 2011 to December 2015. Findings of this study will help health officials monitor trends in hemoglobinopathy disorders over time. This data will eventually contribute to ascertaining the effectiveness of current prevention and control efforts and provide information useful for policymakers interested in reducing the prevalence of hemoglobinopathy disorders.

2. Methods

2.1. Study design

A secondary data analysis was performed using data from the PMSGC program, housed within the Saudi Ministry of Health's Genetic Department. Genetic screening data was obtained for all 12,30,582 individuals seeking to obtain a marriage certificate between the periods of February 2011 to December 2015. In February 2011, the program began computerized data entry.

Blood samples were taken, the results were shared with examinees, and genetic counseling was given. The database included demographic information as well as genetic test results for SCD and β-thal allowing classification of disease status positive, negative, or trait [1].

2.2. Data source – Premarital screening and genetic counseling program

Saudi Arabia launched its premarital screening and genetic counseling program in 2004. A royal decree issued in 2003 mandated premarital screening for the genetic diseases β-thal and SCD as a requirement to obtain marriage certifications [13]. Designated health centers were established for the program and equipped with medical supplies, personnel, and laboratory services [2]. There are currently 125 premarital health-screening centers across Saudi Arabia, all of which report data to the Ministry of Health (MoH), Department of Genetic Diseases [14]. The program offers free testing and counseling for couples looking to get their marriage certificate [3].

The PMSGC program not only identifies genetic blood diseases but also includes some infectious diseases such as hepatitis B, C and Human Immunodeficiency Virus. [13]. After these screenings, couples are provided with medical consultation in order to explain their chances of transmitting these diseases to their partner or future children, helping them plan healthy family outcomes [13].

For each partner in the health care center setting, the assigned program staff collects basic demographic information along with a medical history and general examination [13]. Hemoglobinopathy screening includes complete blood counts (CBC), peripheral blood film, reticulocyte count, high-performance liquid chromatography (HPLC) and sickling test for all the blood samples (in EDTA anticoagulant) [7]. The HPLC test is performed even if CBCs are normal. Several hemoglobinopathy disorders can be detected from this analysis such as β-thal, SCD, and different variations of hemoglobin-like HbC [4]. β-thal trait diagnosis is considered if a person has a Mean Corpuscular Volume (MCV) of <80 fL and/or a Mean Corpuscular Hemoglobin (MCH) of <27 pg, and a hemoglobin A2 level of >3.2% [15]. For diagnosis of the sickle cell trait, the test must show the presence of HbS with positive sickling [7]. Iron studies and serum ferritin, and DNA analysis are not routinely done along with the diagnosis of a-thal due to their low clinical significance in most of the cases [16,17].

2.3. Ethical considerations

The dataset was obtained from the data source in de-identified format. No patient identifiers were included, and a unique ID was used for each case in the dataset. A protocol was followed to protect the privacy and rights of patients. The study team fulfilled administrative and ethical approval requirements. This study was granted review exemption status by the Institutional Review Board (IRB) of Emory University.

2.4. Study variables

The variables included in this study were based on the 2011 study [8]. The dataset included the following variables: a unique identifier to differentiate each individual in the data set, city, age (years), gender (male/female), test results for β-thal major, β-thal trait, SCD, and SCT (Positive/Negative), year of testing and doctor notes.

2.5. Data management

Data was received as separate files with multiple lines per person reflecting each disease result for each individual, one file containing the positive test results and eight files containing the negative test results in the raw datasets, which there were approximately 1,54,336 observations in the positive file, and almost 75,22,356 observations in the negative files. Data was received in Excel format and analyzed using SAS 9.4 (SAS Institute Inc., Cary, NC). All subsequent data management, handling and statistical analyses were done using a terminal-end connection to a High Performance Computing Cluster at Emory University for further analyzing the data and saving results.

The SAS dataset was thoroughly examined for integrity, inconsistencies, inaccuracies, and invalid entries and changes were made to correct data errors and recode variables as needed. "Region" was recoded from its original 20-level variable representing health districts to a 13-level variable representing administrative districts, because population counts (denominators) were only available for administrative regions in Saudi Arabia. Saudi Arabia is divided into thirteen administrative regions: Al-Jouf, Asir, Baha, Eastern region, Hail, Jizan, Maddinah, Makkah, Najran, Northern Borders, Qasim, Riyadh, and Tabouk These regions are further subdivided into twenty health regions according to Ministry of Health [18]. Reclassifications in the variable "City" were made to be consistent with the changes made in "Region". Tests for disorders/diseases

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