Review Article

Epidemiology of hereditary anemias in Saudi Arabia

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INTRODUCTION

Hereditary anemias constitute a significant burden over the different healthcare systems and the affected patients. It has been associated with different morbidities and can even lead up to death. The epidemiology of these anemias is different across the different populations, and many variations were recorded for the different populations as genetics play a significant role. Furthermore, these genes...
have been associated with ethnicities and the skin color of the populations at risk. Accordingly, different investigations aimed to assess the epidemiology of the different hereditary anemias worldwide.²

In Saudi Arabia, the prevalence rates of hereditary anemias are remarkably high compared to other countries.³⁻⁴ For instance, estimates show that the prevalence of thalassemia constitutes one of the highest rates globally. Furthermore, it has been demonstrated that epidemiology significantly differs between the different regions across the Kingdom, and therefore, many epidemiological investigations were conducted. In this context, it has been demonstrated that the prevalence of thalassemia ranges from 0.4% to 5.9% in the Northern and Eastern regions, respectively. In another context, the epidemiology of sickle cell disease is also interesting in the different settings of Saudi Arabia as different studies indicate the increasing prevalence of the condition and changing epidemiology.⁵⁻⁶ However, evidence from these studies is scattered all over the literature, which might be overlapping and difficult to interpret. In the present literature review, we aim to discuss the epidemiology of the different hereditary anemias that were previously investigated in the literature by Saudi-based studies.

METHODS

To retrieve relevant studies, we conducted an extensive literature search of the Medline, Cochrane, and EMBASE databases which was performed on 27th September 2021 using the medical subject headings (MeSH) or a combination of all possible related terms, according to the database. To avoid missing potential studies, a further manual search for papers was done through Google Scholar, while the reference lists of the initially included papers. Studies discussing the epidemiology of the different hereditary anemias were screened for useful information, with no limitations posed on date, language, age of participants, or publication type. Only Saudi-based studies were included.

DISCUSSION

Many epidemiological studies have assessed the prevalence of the different hereditary anemias in Saudi Arabia. These studies indicate the high prevalence of hereditary anemias and blood-related disorders in Saudi Arabia. Therefore, it has been demonstrated that different screening programs were inaugurated for better detection and adequate screening of these blood disorders to reduce the estimated high prevalence rates. Such approaches were also reported in previous countries which indicated the efficacy of these modalities in increasing the awareness and knowledge levels of the different populations about the disease and how to potentially reduce the exposure to the associated risk factors among these populations.

It has been estimated that the prevalence of hemoglobin across the Saudi populations based on reported from the World Health Organization (WHO) ranges between 6-10%, which is also similar to other countries in the Middle East, including Sudan, Morocco, Iraq, Oman, Syria, Qatar and Yemen. These rates were lower than the >10% rate that was estimated for Bahrain (13%), and Cyprus (17%). This indicates the high prevalence of hemoglobinopathies in Saudi Arabia.⁷ The prevalence of glucose-6-phosphate dehydrogenase deficiency (G6PD) in Saudi Arabia was estimated to be 13% among Saudi males, which is considered a relatively high prevalence rate when compared to other rates of populations within the same region.⁸⁻⁹ For instance, estimates show that the prevalence of the disease is 7-10% among male Cypriots, 24% among male Bahrainis, and 62% among male Jews in Kurdistan.¹⁰⁻¹¹ Estimates indicate the high prevalence of G6PD among the different global communities, as it has been reported that the conditions affect millions of people worldwide.¹²⁻¹⁴

Evidence indicates that patients in the Central and Western African communities have been reported to have the highest prevalence rates of sickle cell syndromes. However, it has been furtherly demonstrated that India and other countries within the Arabian peninsula also have high prevalence rates related to sickle mutations (due to hemoglobin S). The Mediterranean littoral was also reported to have high prevalence rates of these diseases. It has been demonstrated that the mutations resulting in the development of this disease in Saudi Arabia have been significantly associated with the disease from Africa based on previous haplotype analysis.¹⁵ As a result of the significant resistance to the hemoglobin S–containing erythrocytes against P falciparum, the development of the mutations has been attributed to this event in Saudi Arabia and other countries.¹⁶ It has been furtherly demonstrated that some subpopulations living in the different Arabic countries have specific characteristics of the disease. For instance, evidence indicates that the prevalence of hemoglobin S in oasis dwellers in Saudi Arabia, Israel-related Arabs, and Eti-Turks, might be up to 25% in these populations.¹⁷⁻¹⁹ Certain populations in Cyprus and Greece might also have higher prevalence rates of hemoglobin S, which has been reported to be up to 30% in some of these villages.²⁰⁻²¹ Furthermore, genetic drifting from different African and Middle Eastern populations has been reported within different analytic investigations to be correlated with rare cases of homozygous sickle cell disease in white populations in North America and other European countries.²⁰⁻²²

The highest prevalence rates are estimated to be for sickle cell disease in Saudi Arabia. An estimated prevalence rate of 5% was reported across the Kingdom based on data from the premarital screening and genetic counseling program between 2011 and 2015. Furthermore, evidence also indicates that sickle cell disease accounted for most of the cases among this population. Furthermore, the trend of the prevalence of the disease was constant during this period. A total number of cases of 1,38,145 per year has been estimated for sickle cell disease and trait. Estimates show
that per 1000 population, the prevalence of sickle disease ranged between 3-4, while the prevalence of sick cell trait ranged between 42-46. Accordingly, it has been demonstrated that the prevalence rate has slightly increased over the years, which might be attributable to the significant improvements in the quality of care for these patients, contributing to a remarkable improvement in the disease-related survival rate. Therefore, studies indicated that many patients with these conditions usually live until marriage age.

Many risk factors can attribute to the development of sickle cell disease. Among these, malaria endemicity is an important factor, and evidence in Saudi Arabia indicates that the regional distribution of malaria is consistent with the regional prevalence pattern of sickle cell disease in these regions. It should be noted that developing sickle cell disease might have a protective effect against malaria morbidities and give the affected patients with malaria a survival advantage. Accordingly, some reports indicated that better survival rates and prolonged life expectancy are usually observed among patients suffering from malaria, which is attributable to developing sickle cell disease. The clinical characteristics of patients suffering from homozygous hemoglobin S vary significantly based on the characteristics of the affected patients and the ethnicities where these patients come from. In general, evidence indicates that patients living in Arabic countries usually have milder characteristics than has been demonstrated among patients living in Africa. However, evidence also shows that some Arabic patients might have severe diseases and develop malignant characteristics. Elevated levels of hemoglobin F might be co-inherited in these patients and are the main etiology that attributes to the development of these severe events as hemoglobin F usually leads to a significant inhibition in the polymerization of hemoglobin S. Preserved splenic functions were also reported among some patients in Saudi Arabia with homozygous hemoglobin S, particularly among patients that concomitantly suffer from α-thalassemia. However, it has been shown that the morbidity in these Arabic countries and Saudi Arabia causes a significant burden on the affected population and healthcare systems.

Recent evidence indicates that the trends of β-thalassemia are significantly decreasing over the past years. On the other hand, it has been demonstrated that the prevalence trends of sickle cell disease is constant over the past years. It should be noted that not many investigations have assessed the trends of these disorders across the Kingdom despite the wide availability of data from the premarital screening and genetic counseling program. Globally, evidence indicates that thalassemia is estimated to be the most common genetic disorder. Furthermore, in Saudi Arabia, α-thalassemia has been reported to be the most prevalent hemoglobinopathy disorder across the Kingdom. In the Eastern region in Saudi Arabia, Mehdi et al reported that 45% of these individuals are heterozygous for developing α-thalassemia. It should be noted that the premarital screening and genetic counseling program did not include this type of anemia within its statistics, and therefore, it was not adequately reported among any previous investigation, and not much data are widely available regarding it. This might be attributable to the fact that there are no currently validated biochemical diagnostic tests to diagnose the carriers of α-thalassemia adequately. It has been furtherly demonstrated that red cell morphology can be relatively rationale in hemoglobin electrophoresis. On the other hand, it has been demonstrated that the prevalence of β-thalassemia accounts for the rest of the total prevalence rate of thalassemia across the Kingdom. The previous investigation by Alsaeed et al that estimated the trends of hemoglobinopathy disorders between 2011 and 2015 in Saudi Arabia based on data from the premarital screening and genetic counseling program. The authors demonstrated that based on this data, β-thalassemia is considered a high-risk disease for the Saudi population, with an estimated prevalence rate of 1.4%. β-thalassemia major accounted for most of these cases, while carriers accounted for the minimal proportion (1.3%). A similar investigation was also conducted by Alswaidi et al and analyzed data from the first years of the premarital screening and genetic counseling program from 2004-2006 and also reported similar findings. However, it should be noted that the prevalence rates of carriers were different among the two investigations, although the total prevalence rate was similar between them. The estimated prevalence rate for carriers was found to be 3.2%. Furthermore, regional variations were also observed across the different regions in Saudi Arabia. It has been demonstrated that the highest prevalence rates were observed in a belt pattern from the West to the East. Consanguineous marriage has been reported to be an important risk factor for the high prevalence of β-thalassemia and sickle cell disease across the Kingdom. It has also been shown that the distribution of consanguinity is different across the different regions within the Kingdom. This can also explain the variations in the epidemiological characteristics in these regions. Therefore, healthcare authorities should consider these variations when planning for interventions to achieve enhanced outcomes that suit populations per each region based on the most prevalent risk factor for each population. Evidence indicates that in Jazan and Eastern regions, the highest prevalence rates of β-thalassemia and sickle cell disease have been estimated in these regions since 2004 based on evidence from the premarital screening and genetic counseling program. It should be noted that population awareness is an important factor to consider when planning for adequate interventions against the
Since the publication of the first edition of sickle cell disease genetics, this has been applied in Saudi Arabia. However, the outcomes were not favorable. For instance, studies show that high-risk couple marriages did not decrease despite the inauguration of the premarital testing program and although many of these populations received adequate genetic counseling. Many patients that are physically incompatorable and are at a high risk of developing sickle cell disease and thalassemia do not follow the recommendations about the Ministry of Health against high-risk couple marriage despite the adequate awareness about these recommendations.

CONCLUSION

Recent evidence indicates that the trends of β-thalassemia are significantly decreasing over the past years. On the other hand, it has been demonstrated that the prevalence trends of sickle cell disease is constant over the past years. G6PD is also highly prevalent in Saudi Arabia. However, recent evidence is lacking in the literature and needs to be updated by future investigations. Consanguineous marriage has been reported to be an essential risk factor for the high prevalence of β-thalassemia and sickle cell disease across the Kingdom.

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