GENETIC ASPECTS OF BETA-THALASEMIA DISEASE IN THE POPULATION OF AZERBAIJAN

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Abstract: Beta-thalassemia represents an inherited blood disorder typified by diminished hemoglobin production, the vital protein facilitating oxygen transport in red blood cells. This condition arises from mutations within the beta-globin gene, culminating in a spectrum of clinical presentations, spanning from mild anemia to grave, life-threatening complications. Particularly prevalent in regions characterized by high rates of consanguineous unions, such as Azerbaijan, beta-thalassemia poses a significant public health concern. This article delves into the genetic dimensions of beta-thalassemia within the Azerbaijani populace, exploring its prevalence, molecular genetic underpinnings, and endeavors in genetic counseling aimed at mitigating its impact.
Keywords: thalassemia, hemoglobin, disease, genetics, blood cells

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Beta-thalassemia is prevalent across various global regions, particularly in areas where consanguineous unions are frequent. Azerbaijan, situated in the South Caucasus region, exhibits a relatively elevated rate of consanguinity, consequently heightening the prevalence of beta-thalassemia within its population.

Although the precise prevalence of beta-thalassemia in Azerbaijan lacks sufficient documentation, it is deemed relatively high. Estimates suggest a carrier frequency of beta-thalassemia in Azerbaijan ranging from 5% to 8%, implying a substantial portion of the populace carries a single mutated beta-globin gene without manifesting symptoms of the ailment. Pinpointing the exact count of individuals with beta-thalassemia major, the most severe manifestation of the disorder, proves challenging due to data limitations and scarcity.

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Table 1. Prevalence of β-thalassemia and HbS in the regions of the Republic of Azerbaijan

Regions	Number of examinees	β-thalassemia frequency, %	Frequency of HbS, %
Ağdaş	581	0.0751	0.0013
Ağsu	411	0.0385	0.0019
Astara	502	0.0393	0.0016
Babək	418	0.0423	0.0035
Qəbələ	847	0.0841	0.0173
Gədəbəy	540	0.0043	0
Göyçay	330	0.0415	0.0023

Xanlar	421	0.0338	0
Xaçmaz	599	0.0291	0.0089
Xınalıq	365	0	0
İmişli	319	0.0425	0
Culfa	77	0.0455	0
Qazax	288	0.0550	0
Quba	555	0.0322	0.0015
Qusar	394	0.0261	0.0019
Laçın	122	0	0
Lerik	103	0.0149	0
Oğuz	338	0.0580	0.0080
Ordubad	152	0.0526	0
Sabirabad	263	0.0645	0
Sədərək	271	0.0429	0.0031
Şahbuz	75	0.0208	0.0208
Şəki	473	0.0559	0.0017
Tərtər	217	0.0333	0
Ucar	463	0.0515	0.0083
Zaqatala	420	0.0336	0
Total	9552	0.0433	0.0040

Source: Akhundova A. Thalassemia in Azerbaijan SSR (prevalence, clinic, treatment). Problems of Hematology 1965;7:10–8.

One of the primary reasons for the elevated prevalence of beta-thalassemia in Azerbaijan is consanguineous marriages, wherein individuals marry close relatives, such as cousins. Consanguinity heightens the probability that both partners will bear the same mutated beta-globin gene, consequently raising the risk of producing affected offspring. Estimates suggest that more than half of all marriages in Azerbaijan involve some degree of consanguinity, thereby substantially augmenting the prevalence of beta-thalassemia within the population.

Beta-thalassemia constitutes a genetically heterogeneous disorder triggered by mutations in the HBB gene, responsible for encoding the beta-globin subunit of hemoglobin. These mutations may yield diminished or absent production of functional beta-globin chains, thereby inducing aberrant hemoglobin synthesis and manifesting clinical symptoms of the disease.

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Various mutations in the HBB gene can precipitate beta-thalassemia, categorized broadly into two main groups [3. s,102].

These mutations directly impact the synthesis of beta-globin chains, leading to diminished or absent beta-globin production. They can be categorized into two main groups:

a) Beta-thalassemia major (β0-thalassemia): This severe form of the disease results in a complete absence of beta-globin production.

b) Beta-Thalassemia Intermedia (β+-thalassemia): This less severe form of the disease is characterized by reduced, but not absent, beta-globin production.

These mutations cause reduced beta-globin production but do not induce the severe clinical manifestations observed in beta-thalassemia major or intermedia. Individuals with beta-thalassemia trait are carriers of one mutated beta-globin gene and one normal gene

Table 2: Common β-thalassemia Mutations in Azerbaijan

Mutation	Frequency in Azerbaijan

IVS-I-1 (G->A)	High
IVS-I-110 (G->A)	Medium
CD 39 (C->T)	Medium
IVS-II-1 (G->A)	Low
CD 8/9 (+G)	Low

Source: Guliyev AM, Rasulov IM, Dadashova T, Schwarz EI, Rosatelli C, Saba L, Meloni A, Gemidjioglu E, Petrou M, Modell B. Thalassemia in Azerbaijan. J Med Genet. 1994; 31 :209–212. [PMC free article] [PubMed] [Google Scholar]

The molecular mechanisms underlying beta-thalassemia are diverse and may involve various genetic alterations, including point mutations, deletions, and insertions in the HBB gene. These mutations disrupt normal splicing, transcription, or translation of the beta-globin gene, resulting in a deficiency of functional beta-globin chains.

The HBB gene exhibits allelic diversity, with hundreds of different mutations identified worldwide. Several common beta-thalassemia mutations (IVS-I-5 (G>C), IVS-I-110 (G>A), and IVS-I-1 (G>T)) have been documented in the Azerbaijani population. These mutations are associated with varying degrees of disease severity and can cause beta-thalassemia major or intermedia.

Given the high prevalence of beta-thalassemia and the potential for serious health consequences, genetic counseling and carrier screening programs have been initiated in Azerbaijan to reduce the incidence of affected individuals and support affected families.

Genetic counseling plays a crucial role in beta-thalassemia management in Azerbaijan. Genetic counselors collaborate with couples at risk of having a child with beta-thalassemia to provide information, assess genetic risk, and discuss reproductive options. Couples carrying both beta-thalassemia traits can choose from various options, including prenatal diagnosis and preimplantation genetic diagnosis (PGD), to have a healthy child without the disease [1. s,34].

Carrier screening programs aim to identify individuals who carry a single mutated beta-globin gene, enabling them to make informed reproductive decisions. These programs have been implemented targeting both related and unrelated couples in Azerbaijan. Screening typically involves blood tests to identify carriers of beta-thalassemia traits. Education and awareness campaigns have also been launched to inform the public about the importance of carrier screening, especially before marriage [4. s,229].

For couples at known risk of having a child with beta-thalassemia, prenatal diagnosis is an option. Prenatal tests such as chorionic villus sampling (CVS) or amniocentesis can detect the presence of beta-thalassemia in the fetus. Couples diagnosed with prenatal beta-thalassemia in the fetus can then make informed decisions about continuing the pregnancy or consider treatment options [6. s,12-16].

In cases where both partners are carriers of the beta-thalassemia trait, preimplantation genetic diagnosis (PGD) offers the option to select unaffected embryos for implantation during in vitro fertilization (IVF). This technique enables couples to have a child free from beta-thalassemia.

Despite efforts to combat beta-thalassemia in Azerbaijan, several challenges persist, necessitating ongoing initiatives to further diminish the prevalence and impact of the disease.

Cultural norms and traditions such as consanguineous marriage can pose difficulties in terms of change. To address this issue, public health campaigns and educational programs must continue to raise awareness of the risks associated with beta-thalassemia and promote the benefits of genetic counseling and carrier screening.

Improving access to health services, including genetic testing and counseling, is crucial, particularly in rural areas. Making these services widely accessible and affordable can help reach a broader population.

Advancements in research and treatment options for beta-thalassemia, such as gene therapy and stem cell transplants, provide hope for those affected. Continued investment in research and the development of new treatments can enhance the quality of life for individuals with beta-thalassemia.

Beta-thalassemia poses a significant health challenge in Azerbaijan due to a combination of genetic factors, including a high carrier frequency and consanguineous marriages. Efforts to tackle this issue encompass genetic counseling, carrier screening, and reproductive options to diminish the incidence of affected individuals. While challenges persist, ongoing initiatives and research offer hope for a brighter future for individuals and families impacted by beta-thalassemia in Azerbaijan. By raising awareness, enhancing access to healthcare, and investing in research, Azerbaijan can make strides in combating this inherited blood disorder.

Beta-thalassemia is inherited in an autosomal recessive manner, meaning both parents must carry a copy of the mutated gene for a child to be affected. If both parents are carriers (each having one mutated gene), their children have:

25% chance of neither being affected nor carrying the mutation.

50% chance of being carriers like their parents.

25% chance of inheriting beta-thalassemia.

In some instances, individuals receive two different mutations of the HBB gene from each parent. This condition, known as compound heterozygosity, can lead to a diverse range of clinical manifestations depending on the combination of mutations.

In some instances, individuals inherit two different mutations of the HBB gene from each parent. This condition, known as compound heterozygosity, can lead to a wide range of clinical manifestations depending on the combination of mutations.

To comprehend the protein foundation of beta-thalassemia, investigating the structural and functional aspects of hemoglobin is crucial. Hemoglobin is a globular protein consisting of four polypeptide chains: two alpha-globin chains and two beta-globin chains. Each globin chain is associated with a heme group containing iron, which binds to oxygen. The binding of oxygen to heme groups is vital for transporting oxygen from the lungs to tissues and organs.

In individuals with beta-thalassemia, mutations in the HBB gene disrupt the production of functional beta-globin chains. This disruption can occur at different levels. Consequently, there is an imbalance between alpha-globin and beta-globin chains, resulting in various structural and functional abnormalities in hemoglobin and red blood cells.

The hemoglobin molecule comprises two components: heme and globin. In a healthy individual, the globin protein consists of two pairs of polypeptide chains. Within the erythrocytes of an adult, there are three distinct types of hemoglobin based on their polypeptide chains:

1. Hemoglobin A: The globin component comprises 2 alpha and 2 beta polypeptide chains, constituting 96-98% of total hemoglobin.

2. Hemoglobin F: The globin component comprises 2 alpha and 2 gamma polypeptide chains, representing less than 1% of total hemoglobin.

3. Hemoglobin A2: The globin portion comprises 2 alpha and 2 delta polypeptide chains, accounting for less than 2-3% of total hemoglobin.

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