GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY IN AZERBAIJAN: HISTORICAL EPIDEMIOLOGY, GENETIC VARIATION AND FUTURE RESEARCH NEEDS

Alisafa Kamran Velizadeh
Physician-Therapist, Medical Service, Police Academy of the Ministry of Internal Affairs, Azerbaijan

e-mail: Dctrelisafa@gmail.com
https://orcid.org/0009-0000-5328-5730

Received 23.06.2025
Accepted 14.08.2025

Abstract: *Introduction: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is one of the most common hereditary enzyme diseases in the world. It can manifest as neonatal hyperbilirubinemia, favism, and drug-induced hemolytic anemia due to the weakening of the erythrocyte defense against oxidative stress.*
Objective: *To analyze the epidemiological and genetic characteristics of G6PD deficiency in Azerbaijan based on historical and modern sources and to identify future research directions.*
Keywords: *G6PD deficiency, epidemiology, Azerbaijan, favism, hemolytic anemia*

Introduction

The enzyme glucose-6-phosphate dehydrogenase (G6PD) ensures the production of NADPH in the pentose-phosphate pathway and plays an important role in protecting erythrocytes from oxidative stress. Deficiency of the enzyme causes erythrocyte damage and hemolysis. It occurs in more than 400 million people worldwide. [1, 7]

The main reason for the widespread prevalence of G6PD deficiency is related to malaria. People carrying this gene mutation (especially female carriers) had a lower risk of contracting malaria. As a result, this trait has been more preserved throughout history and has been genetically transmitted among the population. [2]

The study of G6PD deficiency in Azerbaijan was mainly conducted during the USSR. These studies revealed a high carrier frequency in the Sheki, Absheron and Zagatala regions. However, the lack of modern molecular-genetic studies creates an epidemiological gap. [3, 4, 5]

Methodology

The article is based on a literature review. Sources used:

- Articles published in the journal Genetics during the USSR (1977, 1980, 1985).
- Monographic work in Azerbaijani: Hereditary hematological diseases are widespread in Azerbaijan.
- Global epidemiological study: Howes R.E. et al., PLoS Medicine, 2013.
- Data from the international organization WHO.

Results and discussion

Epidemiology: In a study conducted among schoolchildren in the Sheki region, the hemizygote frequency was 11.1%, and the heterozygote frequency was 12.9%. In the village of Gobu in Absheron, an allele frequency of 3.6% and three different new forms were detected. [4-5]

According to monographic data, G6PD deficiency is most often observed in the Agdash, Goychay, Sabirabad, Imishli regions, moderately in Gazakh, Khachmaz, Sheki, Lankaran, and to a lesser extent in Guba, Gusar, Lerik. In general, a high prevalence of G6PD deficiency is noted in 17 regions included in the malaria belt of the country. [6]

Genetic features: The most common mutation in the Azerbaijani population is the G6PD Mediterranean or Mediterranean variant. This mutation predisposes to severe hemolytic seizures. In studies conducted in Sheki, 6 additional new mutant alleles were also noted. [1-3]

Clinical features:

- Neonatal hyperbilirubinemia: Some of the widespread jaundice cases in Azerbaijan may be related to G6PD deficiency.
- Favism: Acute hemolysis is possible after eating beans (fava).
- Drug induction: Sulfonamides, nitrofurantoin, dapsone, and antimalarials carry a risk.
- Infections: Hemolytic seizures can occur against the background of oxidative stress. [1, 8, 9]

Military-medical implications: Following recent amendments to the national military-medical examination regulations, the evaluation of hereditary hemolytic disorders has been further clarified and standardized.

Within this updated framework, conditions associated with hemolytic anemia-including erythrocyte membrane disorders (such as hereditary spherocytosis), intracellular enzyme deficiencies (including G6PD deficiency) and hemoglobinopathies-are assessed under a unified classification system.

Although G6PD deficiency is not a structural membrane disorder, it is considered within the same regulatory category due to its potential to precipitate hemolytic episodes, in clinically significant cases, such conditions are generally regarded as incompatible with compulsory military service in peacetime, while in wartime they may be classified as limited fit depending on the degree of functional impairment. [10]

Cardiological and surgical aspects:

- Antiplatelet therapy: Low-dose aspirin and clopidogrel are safe.
- Dual antiplatelet therapy: Can be applied with a standard protocol after stenting.
- Anticoagulants: The use of Heparin, LMWH (Low Molecular Weight Heparins) and DOAC (Directly Acting Oral Anticoagulants) does not carry any additional risk. [1]

Discussion: The available literature shows that there are some scientific studies on G6PD deficiency in Azerbaijan. Studies published in the journal Genetics during the USSR revealed a high carrier frequency in Sheki, Absheron, and other regions, and also described the existence of several new mutant alleles. In addition, monographic works prepared in Azerbaijani also provided information on the prevalence of G6PD deficiency in various regions of the country. [3-5]

However, most of these studies date back to the 1970s–1980s and are mainly based on classical biochemical methods (erythrocyte enzyme activity, electrophoresis, etc.). Large-scale epidemiological studies conducted using modern molecular-genetic approaches (PCR, DNA sequencing, mutation mapping) have not yet been carried out.

Therefore, the actual frequency, mutation spectrum, and precise regional distribution map of G6PD deficiency in Azerbaijan are unknown. Despite the widespread observation of neonatal hyperbilirubinemia, there is no G6PD screening program in the country for newborns. This leads to diagnostic gaps in clinical practice.

Although there are mapping projects on G6PD deficiency on a global scale, Azerbaijan is still one of the countries in this map where new scientific research is still in serious need. This situation necessitates the conduct of new studies in the country, the implementation of neonatal screening, and the consideration of G6PD deficiency in health policy.

Conclusion

G6PD deficiency in Azerbaijan has been confirmed by historical studies and is closely related to malaria endemic areas of the country. The real situation is not fully understood due to the lack of modern epidemiological and molecular genetic studies.

It is important to conduct large-scale screening and genetic analysis in different regions of Azerbaijan in future studies. The author is open to international and local cooperation in this area.

References

1. Cappellini M.D., Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. *Lancet*, 2008, V. **371(9606)**, p. 64–74.
2. Howes R.E., Battle K.E., Satyagraha A.W., Baird J.K., Hay S.I. G6PD deficiency: global distribution, genetic variants and associations with malaria. *PLoS Med*. 2013, V. **10(4)**, e1001339.
3. Krasnopol'skaia K.D., Shatskaia T.L., Filippov I.K., Annenkov G.A., Zakharova T.V. Genetic heterogeneity of G6PD deficiency: mutant alleles of G6PD in the Shekii district of Azerbaijan. *Genetika*, 1977, V. **13(8)**, p. 1455–1461.
4. Krasnopol'skaia K.D., və b. Frequency of G6PD deficiency among schoolchildren in Sheki. *Genetika*. 1980, V. **16(7)**, p. 1262–1268.
5. Krasnopol'skaia K.D., və b. G6PD deficiency in Absheron (Kobi). *Genetika*. 1985, V. 21(9), p. 1452–1457.
6. Azerbaijan National Academy of Sciences. Hereditary hematologis diseases prevalent in Azerbaijan. Baku 1990.
7. WHO. Glucose-6-phosphate dehydrogenase deficiency.
8. Luzzatto L., Arese P. Favism and glucose-6-phosphate dehydrogenase deficiency. *N. Engl. J. Med*. 2018, V. **378(1)**, p. 60–71.
9. Sirchia G., Zanella A., Barosi G. Clinical management of G6PD-deficient patients. *Semin Hematol*. 1990, V. **27(1)**, p. 70–81.
10. Cabinet of Ministers of the Republic of Azerbaijan, regulation on Military-Medical Examination. Resolution No. 59, February 29, 2008 (as amended). Available from: https://e-qanun.az