

PREVALANCE OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE DIFICIENCY IN CHILDREN WITH ACUTE HEMOLYSIS AT LATAKIA UNIVERSITY HOSPITAL

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Article Received on 24/06/2025

Article Revised on 14/07/2025

Article Accepted on 04/08/2025

ABSTRACT

Introduction: G6PD deficiency is one of the most common human enzyme defects, affecting more than 500 million people worldwide. It is an X-linked genetic disease that affects males more than females. Severe hemolytic anemia is the most important clinical manifestation of G6PD deficiency, which may be caused by several inciting factors, the most important of which is the consumption of beans. **Objectives of the Research:** Primary Objective: To determine the prevalence of G6PD deficiency as a cause of acute hemolysis in children attending the emergency department aged 6 months to 12 years. Secondary Objectives: Determine the severity of the deficiency. • Identify the most important factors that trigger hemolysis. • Identify the most common clinical manifestations. **Methods:** A descriptive-cross-sectional observational study during the period from(March 2024 to March 2025) at Lattakia University Hospital- Syria. The study included 115 children who had acute hemolysis and met the inclusion criteria. A detailed medical history was taken and G6PD levels were measured 4 months after the occurrence of a hemolytic episode. **Results:** Among 115 children with acute hemolysis, cases (57.4%) were diagnosed as G6PD deficiency. Most cases were in males (75.8%) compared to (24.2%) in females. Fava beans were the most common triggering factor for the hemolytic episode. Pallor, jaundice, and dark urine were the most common clinical symptoms. Moderate enzyme deficiency was the most common (62.1%). **Conclusion:** G6PD deficiency is an important cause of acute hemolysis in children. Diagnosis and appropriate preventive measures should be established.

KEYWORDS: G6PD enzyme, G6PD deficiency, hemolytic anemia, favism.

INTRODUCTION

G6PD deficiency is defined as one of the most common human enzymatic disorders, caused by genetic mutations in the G6PD gene linked with X chromosome.^[1] Hemolytic anemia is a group of disorders characterized by the destruction of red blood cells at a rate faster than the ability of the bone marrow to product. It can be caused by genetic or acquired factors.^[2] Favism occurs after the consumption of fava beans in individuals with G6PD deficiency.^[3]

G6PD enzyme is essential for converting NADP to NADPH via the pentose phosphate pathway. The conversion of NADP to NADPH is crucial for the production of glutathione, which is an important antioxidant that helps protect red blood cells from oxidative stress.^[4]

G6PD deficiency is one of the most common forms of hemolytic anemia, especially among males, affecting approximately 10% of the world's population.^[5]

Severe hemolytic anemia is considered the most common clinical manifestation among patients with G6PD deficiency. It usually begins with typical symptoms and signs such as feeling tired, abdominal pain or lower back pain, jaundice, and changes in urine color.^[6] The clinical signs and symptoms of hemolysis typically appear within 24-72 hours after exposure to an oxidative substance (such as broad beans, medications, etc.), and the hemolysis worsens depending on the concentration of the oxidative substance in the blood.^[7] The consumption of broad beans (fava beans) is the most common trigger for hemolysis in patients with G6PD deficiency, followed by medications and then infections.^[8]

G6PD deficiency is a significant cause of severe hemolytic anemia among children, and episodes can be life-threatening in rare cases. In this study we aimed to determine the prevalence of G6PD deficiency as a cause of severe hemolytic anemia among children presenting to the Emergency Department at Lattakia University Hospital and we teied to assess the severity of deficiency, to identify the most common triggering

factors for hemolysis, and mark the most frequent clinical manifestations.

METHODS AND PATIENTS

Study design

Descriptive Cross-Sectional Observational Study.

Participants

The study included all patients presenting to the Pediatric Emergency Department at Latakia University Hospital.

Data collection

Inclusion Criteria: All children referred to the Pediatric Emergency Department with a severe hemolytic crisis, aged over 6 months. After obtaining informed parental consent, the following procedures were performed for all children included in the study: a detailed medical history (age, gender, history of glucose-6-phosphate dehydrogenase deficiency (G6PD), recurrence of hemolytic crises, triggering factors for the crisis, clinical symptoms and signs, and the need for blood transfusion). G6PD activity assay was conducted 4 months post-crisis.

Statistical analysis

Descriptive statistical methods were used for the studied variables, including measures of central tendency, measures of dispersion, frequency distributions, and percentages. Percentile values were also included. The data were presented in tabular and graphical formats. The IBM SPSS Statistics software (Version 25) was used to calculate statistical coefficients and analyze the results.

Ethical Considerations

The study protocol was reviewed and approved by the ethics committee at the Faculty of Medicine – Latakia University, ensuring compliance with ethical standards for research involving human subjects. Informed consent was obtained from all participants prior to data collection, with assurances provided regarding confidentiality and the voluntary nature of participation.

RESULTS

During the study period (2024-2025), the number of cases of severe hemolytic anemia that visited the pediatric emergency department at Latakia University Hospital was 132. Seventeen of cases were excluded due to incomplete data. The research sample included 115 children who visited the Pediatric Emergency Department with a severe hemolytic crisis and met the inclusion criteria for the study. The children's ages ranged from 11 months to 12 years, with a mean age of 4.63 ± 2.9 years.

About 63.5% of the studied sample were males, and 36.5% were females.

About 61.7% of the studied cases were aged from 2-6 years, 31.3% were older than 6 years, and 7% were less than two years.

The prevalence rate of G6PD deficiency reached 57.4% of the cases admitted to the emergency department with hemolytic episodes. We observed that the highest percentage was for G6PD deficiency at 57.4%, followed by sickle cell anemia at 27.8%, thalassemia at 12.2%, and other causes at 2.6%. We also noticed that the prevalence of G6PD deficiency among males was higher at 75.8% compared to 24.2% among females (Figure 1).

Moderate G6PD deficiency is the most common, accounting for 62.1%, while severe deficiency was 24.3%. The percentage of severe deficiency was higher among females than among males as seen in Table (1).

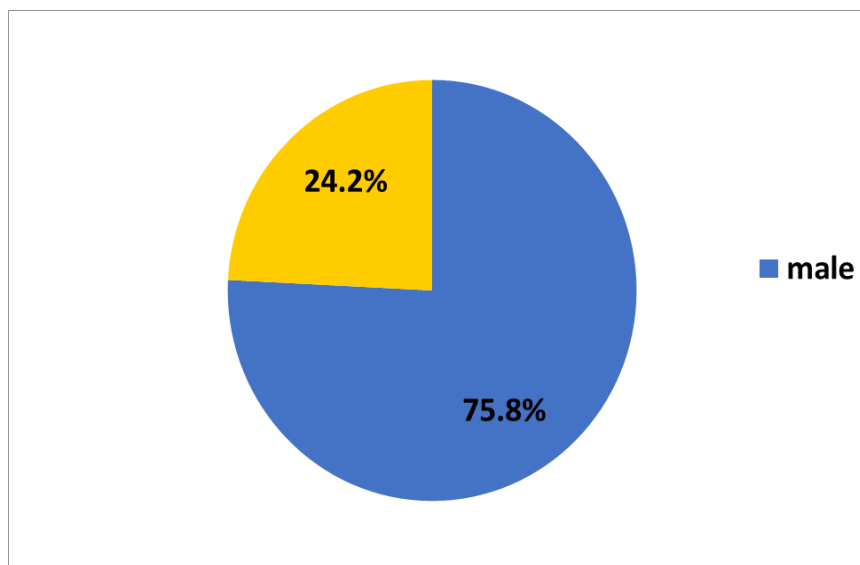
The results indicate that the provoking factor for the attack was food in 93.9%, including bean consumption at 78.8% and other foods at 19.7%. Infection was the least common cause, accounting for 1.5%.

The most common clinical symptoms and signs among the studied cases were pallor, with a prevalence of 100%, followed by dark urine at 87.9%, and jaundice at 84.8%. About 75.8% of the cases with G6PD deficiency experienced a hemolytic crisis for the first time and 54.5% of G6PD deficiency cases had a positive family history of hemolytic crisis.

The results showed that 84.8% of the cases with G6PD deficiency anemia received blood transfusions once, 9.1% received transfusions more than once, and 6.1% did not require any blood transfusions. Additionally, hemoglobin levels among these children ranged from 4.10 to 8.70, with a mean of 6.20 ± 0.9 .

Table 1: The distribution of G6pd deficiency according to the degree of deficiency and sex.

Degree of Deficiency	Frequency	Proportion	Male	Female
Mild	9	13.6%	6(12%)	3(18.8%)
Moderate	41	62.1%	33(66%)	8(50%)
Severe	16	24.3%	11(22%)	5(31.2%)

**Figure 1: The Distribution of Sample According Sex.**

DISCUSSION

In the current study, the prevalence of G6PD deficiency among hemolytic cases was 57.4%, which is higher than the rates reported in studies by Qasim et al. (2019) in Saudi Arabia^[9] and Amiwero et al. (2012) in Nigeria, where the percentages were 30% and 43%, respectively. The reason for this difference is likely due to the inclusion of age groups starting from 1 day old in the previous studies, which considered hemolytic events caused by ABO incompatibility and Rh incompatibility. In contrast, the current study included children starting from 6 months old. Additionally, a study conducted by Badr et al (2020) in Egypt.^[10] Which aimed to identify patterns of hemolytic anemia in the emergency department, found that 53.1% of the hemolytic patients reviewed had G6PD deficiency. This percentage is similar to that of the current study, where children's ages ranged from 3 months to 15 years. two similar studies conducted by Kamali and colleagues in 2022 and 2023 in malaria-endemic areas of southern Iran, the prevalence of G6PD deficiency among children presenting with hemolytic symptoms was 24.7% and 6.7%, respectively.^[11] Meanwhile, in the studies by Isaac et al. in 2013 in Nigeria and Jha et al.^[12] in 2022 in Nepal, the prevalence rates were 14.4% and 9.3%, respectively, which are significantly lower than in the current study.^[13] These previous studies measured enzyme activity in patients regardless of the presence of hemolytic symptoms, whereas the current study focused only on cases of severe hemolytic anemia.

G6PD deficiency is the most common enzymatic disorder worldwide, with a highly variable prevalence,

ranging from 0% among Native Americans to over 20% in parts of Africa and Asia. Males constitute the majority of G6PD deficiency cases, with 50 male cases accounting for 75.8%, compared to 16 female cases, which make up 24.2%. This is consistent with all previous studies and is explained by the fact that G6PD deficiency is a hereditary disorder linked to the X chromosome. However, the relatively high percentage of affected females in the current study is likely due to the widespread practice of consanguineous marriages.

The highest prevalence of G6PD deficiency was observed in the age group of 2-6 years, accounting for 74.3%. This aligns with the study by Ajlouni in 2016 in Damascus, where the highest percentage of deficiency was found in children aged 2-5 years, at 60%.^[14] It also corresponds with the studies by Armishty et al. in 2023 in Iraq and Jha et al. in 2022 in Nepal, where the highest percentages were among children aged 1-5 years. Usually, pyruvate kinase deficiency (fouling) is diagnosed at this age range with exposure to hemolytic triggers and the introduction of diversified nutrition to infants, in the absence of an early screening program for newborns in our country.

In the study by Badr et al. in 2020 in Egypt, most cases of G6PD deficiency were in children under two years old, accounting for 56.2%. Badr attributed this to early consumption of fava beans and the widespread consumption of beans by breastfeeding mothers.

The current study demonstrated that eating fava beans is the most common trigger factor for hemolysis in the

studied sample, with a rate of 78.8%. This is consistent with studies by Ajlouni in Damascus (2015), Kavehmansh in Iran (2016)(15). Badr in Egypt (2020), and Armishty et al. in Iraq (2023). However, in the study by Qasim in northern Saudi Arabia (2019), infections—especially viral—were identified as the main cause of hemolysis, where fava bean consumption is not common in that region.

The first episode of hemolysis occurred in 78.8% of patients with G6PD deficiency, while it was recurrent in 21.2%. The recurrence rate of hemolytic episodes was 18% in the Ajlouni 2015 study, 25.2% in the Qasim 2019 study, and 28.9% in the Badr 2020 study. The higher percentage of recurrent cases is attributed to non-compliance with dietary and medication restrictions.

A family history of hemolysis was negative in 45.5% of the cases, which is lower than the percentages in the Badr study (59.2%) and the Qasim study (64.4%). In contrast, in the Ajlouni and Kavehmansh studies, the family history was negative in 31% and 30.6% of cases, respectively. The absence of a positive family history may indicate the presence of new mutations in the G6PD gene.

Among 50 children, 75.7% had mild to moderate deficiency, while severe deficiency accounted for 24.3%. The severity of G6PD deficiency varies significantly among different ethnic groups. Additionally, polymorphic gene mutations lead to enzyme variants with differing activity levels, resulting in a range of clinical manifestations of the disorder.^[16,17]

Study limitations include a small sample size and the lack of investigation into the prevalence of the disease on a broad geographical scale. Some patients did not adhere to enzyme calibration four months after an hemolytic episode.

CONCLUSIONS

G6PD deficiency is the most common cause of acute hemolytic anemia in children. The condition is more frequently observed in males and in the age group between 2-6 years. Fava (ball beans) is the most important trigger for hemolytic episodes in patients with G6PD deficiency. Mild and moderate enzyme deficiencies were observed in most cases.

We recommend early screening for G6PD deficiency when there is a family history of hemolysis. Further studies are suggested to determine the specific G6PD gene mutations present in our country. Educating parents about avoiding triggering factors, especially dietary and medication-related, is crucial for children diagnosed with G6PD deficiency.

Declarations

Ethical approval and consent to participate: Ethical approval to study was obtained from the Scientific

Research Ethics Committee at Latakia University in accordance with the Declaration of Helsinki.

Consent for publication: Not applicable.

Availability of Data and Materials: All the data generated or analyzed during this study are included in this published article. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests: None.

Funding: None.

Author Contribution: Sarab Gamee, collected the data, checked the quality of the data collection, analyzed and interpreted the data, designed and coordinated the study, undertook and checked the quality assessment, produced the first draft of the manuscript, wrote and edited the manuscript and approved the final manuscript before submission. Souaad Sakkour and Abdulmounaem Ghanem were the supervisor of the project; undertook and checked to the quality assessment, checked the quality of the collected data; analyzed and interpreted the data; checked the quality assessment; edited the manuscript and approved the final manuscript before submission.

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