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Original article

Prevalence of glucose-6-phosphate dehydrogenase deficiency and the potential of neonatal complication prevention

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Abstract

Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common inherited disease. The aim of our study was to assess the prevalence and gender distribution of G6PD deficiency in Jordan and to establish the rate of neonatal morbidity in G6PD-deficient patients compared to healthy neonates. Moreover, the present study aimed to evaluate the neonatal G6PD deficiency screening program.

Materials and methods: This was a retrospective study conducted at a tertiary hospital in Amman, Jordan. All infants born between January 2016 and March 2020 were included. Demographic and clinical data were extracted from the patients' medical records and hospital laboratory databases.

Results: During the study period, 11,128 neonates underwent the neonatal screening program, and 114 (1.02%) did not undergo screening at the appropriate time. Among the included neonates, the overall prevalence of G6PD deficiency in our population was 1.44%, with a higher proportion among males than among females (2.38% vs. 0.36%), with a male-to-female ratio of 7:1. The rate of pathological neonatal hyperbilirubinemia and blood exchange transfusion was significantly higher in patients with G6PD deficiency.

Conclusions: The evidence from this study suggests that our institution's G6PD screening program is a successful program. G6PD deficiency is

prevalent among Jordanian males. It is a major cause of pathological neonatal hyperbilirubinemia and blood exchange transfusion.

Keywords

G6PD deficiency, neonate, screening program, hyperbilirubinemia, exchange transfusion, prevalence.

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Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency causes a spectrum of diseases, including severe anemia and neonatal hyperbilirubinemia [1]. It is caused by a genetic defect in the red blood cell (RBC) enzyme G6PD, which is responsible for the generation of nicotinamide adenine dinucleotide phosphate and the protection of the RBCs from oxidative injury [2].

G6PD deficiency affects around 400 million people worldwide [3]. The prevalence of G6PD deficiency varies widely between countries, as it is more common in certain ethnic groups. Prevalence ranges from 2% in Saudi Arabia and 4.3% in Egypt to 23% in Nigeria [4-6]. In Jordan, few studies have aimed to investigate the prevalence of G6PD deficiency. These studies were conducted either in a closed local community or in a small sample of male patients [7, 8].

G6PD deficiency is an X-linked disorder that primarily affects males. Heterozygous females do not usually develop severe hemolytic anemia due to G6PD deficiency [9].

G6PD-deficient newborns are usually asymptomatic, unless they are exposed to oxidative stress, which can be triggered by foods, such as fava beans or certain drugs and infections. If this is the case, they might develop severe hemolysis [10, 11], causing severe neonatal hyperbilirubinemia, which could potentially lead to bilirubin-induced neurological dysfunction (BIND) [12].

Depending on the prevalence of G6PD deficiency in a population, neonatal screening programs for G6PD deficiency should be established, aiming for early recognition and prevention of its complications [2].

In Jordan, neonatal screening programs started at Jordan University Hospital in the late 1990s for congenital hypothyroid and G6PD deficiency. Shortly after, in the early 2000s, the Ministry of Health started a similar national program. At the hospital, we perform screening of G6PD deficiency by enzyme analysis using venous blood samples.

This study aimed to evaluate the success of our neonatal G6PD deficiency screening program, to assess the prevalence and gender distribution of G6PD deficiency in the Jordanian population, and to investigate the rate of G6PD-related neonatal morbidities.

Methods

Study design

This was a retrospective study conducted by reviewing the medical charts and laboratory database of all infants born at Jordan University Hospital between January 2016 and March 2020. The study was approved by the Deanship of Scientific Research at the University of Jordan, and it received ethical approval from the IRB Committee at the University of Jordan Hospital. The requirement of obtaining consent was waived as the study was a retrospective chart review without the identification of the participants. The study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Data collection

A structured sheet was used for data collection. Relevant demographic and clinical data for each newborn were obtained from their electronic medical records, including G6PD-related neonatal morbidities.

For G6PD deficiency screening, approximately 1 ml of venous blood was collected in sterile

plastic tubes with K2-ethylenediaminetetraacetic acid (K2-EDTA) (BD Vacutainer™).

The collected samples were stored at refrigerator temperature between 2°C and 8°C until processed for a maximum period of 3 days after the collection date. Samples were tested for G6PD deficiency using the MBK G6PD® qualitative assay (ARKRAY Healthcare Pvt. Ltd., India).

Statistical analysis

Data for each studied newborn were entered into a spreadsheet, and statistical analysis was performed using Microsoft® Excel® 2010. Data are expressed as mean ± SD and frequency. Chi-square test was used to evaluate the association between variables, and a p-value < 0.05 was considered statistically significant.

Results

During the study period, there were 23,140 live births in Jordan University Hospital, of which 11,128 neonates returned for screening on time. A total of 114 infants (1.02%) were followed up later than expected, and they represent the dropout rate.

Of the included infants, 5,219 (46.90%) were delivered by cesarean section, and 5,913 were males (53.14%) in the study group. The median gestational age was 38 weeks (SD ± 2 weeks).

The prevalence of G6PD deficiency in our population was 1.44%, with a higher proportion among males than females (2.38% vs. 0.36%, p = 0.00003) (**Tab. 1**).

Among the neonates in the G6PD-deficient group, 31 (19.38%) developed hyperbilirubinemia that required phototherapy, which is significantly higher than that of neonates in the G6PD-normal group (965 [8.80%] neonates; p = 0.000003).

Table 1. Demographic data and rate of G6PD deficiency in screened newborns (n = 11,128).

Variable	Median ± SD/frequency
Gestational age (weeks)	38 ± 2
Birth weight (grams)	3,000 ± 500
Small for gestational age	854 (7.67%)
Male gender	5,913 (53.14%)
Cesarean section	5,219 (46.90%)
Newborns screened late	114 (1.02%)
G6PD deficiency	160 (1.44%)
G6PD-deficient males	141 (2.38%)
G6PD-deficient females	19 (0.36%)

G6PD: glucose-6-phosphate dehydrogenase.

Severe neonatal hyperbilirubinemia requiring exchange transfusion was significantly more frequently noted in G6PD-deficient babies than in G6PD-normal babies (2 [1.25%] vs. 3 [0.03%] babies, p = 0.000004; **Tab. 2**).

Table 2. Clinical outcomes comparison between G6PD-deficient and G6PD-normal newborns.

Variable	G6PD-deficient newborns (n = 160)	G6PD-normal newborns (n = 10,968)	p-value
Male gender	141 (88.13%)	5,772 (52.63%)	0.00003
Family history of G6PD deficiency	8 (5.00%)	19 (0.17%)	0.00004
Pathological hyperbilirubinemia	31 (19.38%)	965 (8.80%)	0.000003
Exchange transfusion	2 (1.25%)	3 (0.03%)	0.000004

G6PD: glucose-6-phosphate dehydrogenase.

Discussion

In Jordan, G6PD deficiency is a common inherited genetic disorder. Based on previous small studies, the estimated male prevalence is 3.6% [7] to 5.5% [8]. However, large cohort studies that investigate G6PD prevalence and evaluate screening programs are lacking.

Our hospital is a university hospital that was established in the late 1970s and is one of the largest tertiary centers in Jordan. It offers primary and complex neonatal care. Almost half of the country's population lives in Amman, as many Jordanians left their hometowns looking for better opportunities in the capital city. Thus, in this study, we consider the Amman population representative of all Jordanian areas.

Our neonatal screening program was established in 1998. This was the first established program in the country and includes screening for congenital hypothyroidism and G6PD deficiency. Screening is usually performed between day 3 and day 7 of life. Screening for hyperbilirubinemia was started 10 years ago. All newborns were screened for hyperbilirubinemia whenever they looked jaundiced or upon discharge, whichever occurred earlier.

The national screening program at the primary health care centers offers screening during the first 2-4 weeks of life, and the parents of newborns at our hospital could choose to be followed up at our center or at the Ministry of Health Primary Care Centers. For the sake of this study, only those

who chose to be followed up at our hospital were included.

The results of the screening tests were saved on the electronic medical files and lab database. Parents of G6PD-deficient newborns are informed and educated about the risk factors and signs of hemolysis. They receive an information sheet that they present to any physician who might provide care to their child. It mainly includes medication that should not be administered or should be administered with precautions. Approximately 114 babies were screened late, resulting in a dropout rate of 1.02%, reflecting the efficiency of our screening program.

In our study, the prevalence of G6PD deficiency was estimated to be 1.44%, which is lower than that in Egypt and Saudi Arabia, with rates of 4.3% and 2%, respectively [4, 5]. The prevalence in males was 2.38%, versus 0.36% in females, with a male-to-female ratio of 7:1. Our proposed prevalence of G6PD deficiency in males was lower than the previously reported prevalence in northern Jordan valley and Irbid of 5.5% and 4.62%, respectively [8]. However, this previous study had a significantly smaller sample size and was conducted in a local closed community. Another study [7] found a prevalence in males of 3.6%, but it also evaluated a smaller sample. In contrast, our study not only had a larger sample size than the previous studies but also was performed in the second largest hospital in Amman, the capital city, where about half of Jordan's population lives. Amman's population is a mixture of Jordanians from all cities; therefore, our numbers can be considered more representative of the Jordanian population than the previously reported prevalence rates.

In our study, the rate of pathological neonatal hyperbilirubinemia requiring phototherapy was higher in G6PD-deficient patients (19.38%) than in G6PD-normal newborns (8.80%). Exchange transfusion was also significantly higher in G6PD-deficient infants than in G6PD-normal babies (1.25% vs. 0.03%, $p = 0.000004$). In Jordan, G6PD deficiency is a major cause for exchange transfusion [13]. In our institution, it constitutes 15% of the hemolytic causes of exchange transfusion [14].

In our study, most infants were screened early, with a mean age of 5.6 days. Screening for G6PD deficiency in neonates during the first week of life is crucial to decrease related neonatal morbidities, and should be coupled with screening for neonatal hyperbilirubinemia [15, 16].

Conclusions

Our neonatal screening program was efficient. Most infants were screened early. G6PD deficiency is prevalent in our community and causes a higher rate of pathological neonatal hyperbilirubinemia and exchange transfusion. Implementing the G6PD neonatal program with screening for hyperbilirubinemia is the key to avoiding a potentially long-term severe complication.

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Declaration of interest

The Authors have no conflict of interest to be declared. This study did not receive any funding.

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