Neonatal Screening for Glucose-6-phosphate dehydrogenase Deficiency in Ardabil Province, Iran, 2018-2019

Afshin Fathi 1, Manouchehr Barak 2, Mahshid Damandan 3, Firouz Amani 4, Rouhallah Moradpour 3,4, Irada Khalilova 3*, Mehdi Valizadeh 5

ABSTRACT
Glucose-6-phosphate dehydrogenase (G6PD) is one of the most common genetic deficiencies that affect approximately 400 million people worldwide. This study aimed to identify neonates with G6PD deficiency in Ardabil province during 2017-2018. This cross-sectional study was conducted on all term and preterm newborns in Ardabil Province from April 2018 to April 2019. The sampling method was census and in study duration, 1044 newborns were entered in the study. For each infant, severe hyperbilirubinemia (total serum bilirubin equal or greater than 300 micromol/L) was tested by the diazo method and G6PD was evaluated by Fluorescent Spot Test (FST). Of all infants, 15 (1.4 %) were diagnosed to have G6PD deficiency by FST. The prevalence of G6PD deficiency was significantly in boys higher than in girls (80% vs. 20%, p=0.001). Of all infants, 97 (9.3%) had jaundice 72 hours after birth that of them 7 neonates (7.2%) had G6PD deficiency. Results showed that the prevalence of G6PD deficiency in this study was less than in other places in Iran that may be because of different ethnicity and demographic features.

1. Introduction
Glucose-6-phosphate dehydrogenase (G6PD) is one of the most common genetic disorders that affect about 400 million people worldwide [1]. A high rate of G6PD deficiency has been reported from the Mediterranean, African and Asian regions [2]. The prevalence of G6PD deficiency in Iran is estimated at 11.5% [3]. Although most affected individuals are asymptomatic, G6PD defense against oxidative damage in all cells of the body by converting nicotinamide adenine dinucleotide phosphate (NADP) to reduced NADP(NADPH) by the hexose monophosphate pathway [4].

In the erythrocytes, the only source of NADP is the hexose monophosphate pathway, therefore, hemolysis and hemoglobinuria can occur in patients with G6PD deficiency which was triggered in most of the patients by certain drugs, infections and fava beans intake [5]. Hyperbilirubinemia is the most common medical problem during the neonatal period; about sixty percent of full-term neonates develop non-hemolytic hyperbilirubinemia. Neonatal jaundice is the earliest manifestation that can be lead to permanent brain injuries, kernicterus and death or is cerebral palsy, if untreated but in most cases is asymptomatic and G6PD deficiency has been determined to be an X-linked recessive. So, it was more common in males than females [6-8].

The higher bilirubin level in newborns...
with G6PD-deficiency could increase the neurological damage than infants with normal G6PD [9]. In a study, has been reported that out of 5% of neonates with G6PD deficiency, develop jaundice in the first three days of life, therefore, early diagnosis of G6PD deficiency is quite important and can be prevented from life-threatening manifestations in neonates [7]. This study aimed to identify neonates with G6PD deficiency in Ardabil province north-west of Iran during 2017-2018 by doing a neonatal screening program.

2. Materials and methods

2.1. Study design and Participants

This screening was conducted on all term and preterm newborns who were born in Ardabil province hospitals from April 2018 to April 2019.

In this cross-sectional study, 1044 newborns were entered in the study. Written consent was taken from all parents of infants. Demographic data including gender, gestational age, birth weight and delivery type were extracted from hospital records of neonates and entered in a checklist. Blood samples were collected for each neonate in an EDTA tube and shipped to the laboratory in a cold chain to G6PD enzyme assay. The test was performed using Fluorescent Spot Test (Zist Takhmir, Company, Iran), and done in a local laboratory. The parents of affected neonates were informed by health workers as soon as possible by a phone interview. The method was a quantitative photometric Enzyme Activity technique (kit Randox, U.K.) with a sensitivity of 154 IU and a normal range of 6.97-20.5 U/gHb. A confirmatory test was done for all G6PD-deficient samples using venous blood within 120 days of birth.

2.2. Statistical analysis

The collected data were analyzed by statistical methods in SPSS version 18. The t-test and chi-squared test were used to determine the relationship between variables. P-value < 0.05 was considered as significant.

3. Results

During one year; from April 2017 to April 2018, we enrolled 1044 live newborns (59.3% boys and 40.7% girls) in the study. Of them, 752 cases (72%) were delivered by the vaginal method. Of all neonates, 91.6% were Term. The average birth weight of them was 3374 gr in the range 1700-4000 gr (Table 1).

Of all infants, 15 (1.4%) were diagnosed to have G6PD deficiency by FST (Fig.1). The frequency of G6PD deficiency among neonates in this study was 15 (1.4%) of them, 12 (80%) neonates were boys and 3 (20%) neonates were girls with a sex ratio of 4:1. The rate of G6PD deficiency was 1.94% and 0.71% in boys and girls, respectively and the difference between the two sexes was significant (p=0.001) (Fig.2).

<table>
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<tr>
<th>Table 1. Characteristics data of studied neonates</th>
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<tr>
<td>subject</td>
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<tr>
<td>Gender</td>
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Out of 1044 neonates, 97 (9.3%) had jaundice 72 hours after birth which of them, 56 (57.7%) were boys and 41 (42.3%) were girls. Of all infants with jaundice, 7 neonates (7.2%) had G6PD deficiency. The frequency of G6PD deficiency in jaundice infants was significantly more than total infants (7.2% vs. 1.4%, p=0.034). Also, the frequency of G6PD deficiency in neonates with jaundice was similar neonates without jaundice (Fig.3).
Fig.1. Frequency of G6PD deficient and sufficient neonates in our study

Fig.2. Frequency of G6PD deficient and sufficient neonates by sex distribution

Fig.3. Frequency of G6PD deficient and sufficient neonates by Jaundice

4. Discussion

G6PD deficiency is the most common human enzyme deficiency in the world. In this study, 1.4% of neonates had G6PD deficiency. The overall incidence of G6PD deficiency in the Iranian population is reported in the range of 10% to 15% by WHO [10]. The rate of G6PD deficiency in Iranpour et al., a study in Esfahan (middle of Iran) was reported about 3.2% which was upper than our study results. The incidence of G6PD deficiency varies markedly in different provinces of Iran from 8.65% to 16.4% in the northern part of Iran (Mazandaran and Guilan Provinces), 12% in the southern part of Iran (Shiraz), 19.3% in the southeastern part of Iran, 2.1% in the center and the north of Iran (Tehran), 2.1% in Northwest of Iran (Tabriz) and 8.4% in Boushehr in the south of Iran [11, 12]. These differences might be because of differences between the Ethnicity of people who live in Iran [11]. In this study, the male-to-female ratio of G6PD deficiency was 4:1. This ratio was reported from 3:1 to 6:1:1 in some studies [13-15]. The frequency of G6PD deficiency in boys and girls was 1.94% and 0.7%, respectively.

In this study, there was a significant association between bilirubin and G6PD in neonates. Out of 15 infants with G6PD deficiency, 9 infants (60%) had hyperbilirubinemia with jaundice which was different from non-icteric infants (8.55%) (P=0.005). There was a significant difference between boys and girls in terms of the G6PD deficiency rate.

Neonatal hyperbilirubinemia of all clinically significant enzyme defects that may be lead to major health concerns including acute Bilirubin encephalopathy, sensor neural hearing loss and even kernicterus [16]. Najib KS et al., reported that the prevalence of severe hyperbilirubinemia in the South of Iran was 15 percent in all of the neonates [17]. Kavehmanesh et al., carried out a study on 2702 infants in Tehran and showed that the incidence of hyper Bilirubinemia was 12.6%. The incidence of hyperbilirubinemia was reported from 1.7% to 12.6% in different studies [18-20]. Reasons for the discrepancies between various studies may be because of the definition of hyperbilirubinemia manner, ethnicity and geographic variations in different populations [21].

One study indicated that G6PD-deficient infants had a higher risk (even 3-fold) of hyperbilirubinemia in comparison to G6PD-normal counterparts. Abolghasemi et al., in a study, reported that 51% of G6PD-deficient infants had hyperbilirubinemia that was significantly higher than the hyperbilirubinemia rate in G6PD-normal infants with 16% [22].
Amoozgar et al., in a study, showed that the prevalence of G6PD in the Iranian population is estimated around 10%-14.9% which was higher than our study results because in our study this rate was about 1.4% [23].

In this study of all neonates with jaundice, 7 neonates (7.2%) had G6PD deficiency and the frequency of G6PD deficiency in jaundice infants was significantly more than total infants (7.2% vs. 1.4%, p=0.034). Sinha et al., in a study, showed that only 2.5% of neonates with jaundice had G6PD deficiency which was lower than our study results [24].

M Abo El Fotoh WM et al., in a study entitled "Prevalence of glucose-6-phosphate dehydrogenase deficiency in jaundiced Egyptian neonates" showed that G6PD deficiency is found to be an important cause of neonatal jaundice and there was a significant positive correlation between the time of appearance of jaundice in days and G6PD levels in G6PD deficient cases. The results of this study were confirmed by our study results because in our study we also resulted that G6PD deficiency can be a probable reason for the occurrence of jaundice in neonates [25].

5. Conclusion

Results of this study showed that the frequency of G6PD enzyme deficiency in neonates with 1.4% was relatively fewer than in other places within the country of Iran. Due to the high frequency of jaundice in G6PD-deficient infants, we suggest a qualitative test of this enzyme deficiency for all icteric neonates toward early diagnosis and prevention of adverse consequences of neonatal hyperbilirubinemia, and also we can suggest that early neonatal screening programs should be essential in these neonates. So, it is recommended that all of the icteric neonates should be evaluated for G6PD activity as well as to test for G6PD deficiency in all neonates, to detect its presence and to prevent its complications such as favism and oxidant drug-induced hemolysis since the test has a low cost.

Abbreviation

G6PD: Glucose 6-phosphate dehydrogenase

NADP: Nicotinamide Adenine Dinucleotide Phosphate

Conflict of interest

None of the authors have any conflict of interest to declare.

Consent for publications

All authors approved the final manuscript for publication.

Availability of data and material

The authors have to declare that they embedded all data in the manuscript.

Authors’ contributions

AF help in study design, doing, MB help in manuscript draft writing, study design, MD help in data collection, FA help in data analysis and manuscript writing, RM help in sampling and data collection, IK help in study design, doing and article drafting, MV help in sampling and data collection.

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Ethical consideration

This study design was approved by the research committee of the Ardabil University of Medical Science and registered by code IR.REC.ARUMS.1397.9310 in the research unit. Also, consent forms were completed for all participants.

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