Glucose-6-Phosphate Dehydrogenase Deficiency and Neonatal Hyperbilirubinemia

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ABSTRACT

Background: Jaundice is affecting over 60-80 percent of neonates in the first week of life. Glucose-6-phosphate dehydrogenase (G6PD) deficiency, which is an important cause of pathologic hyperbilirubinemia, can lead to hemolytic anemia, jaundice and kernicterus. The present study was performed to determine the prevalence of G6PD deficiency among icteric neonates in Shirvan, Iran.

Methods: This descriptive, analytical study was performed by evaluating the medical records of neonates with jaundice, admitted to the neonatal ward of Imam Khomeini Hospital of Shirvan in 2012-2013. All neonates, who were evaluated in terms of G6PD, were included in this study. Data including the clinical signs and symptoms, laboratory test results and maternal history during pregnancy were recorded in the questionnaires. The patients were divided into two groups: with and without G6PD deficiency. The recorded data were compared between the two groups, using t-test and Chi-square test. P-value less than 0.05 was considered statistically significant.

Results: Among 452 admitted neonates, 16 (3.5%) presented with G6PD deficiency. There was no significant difference between the two groups in terms of birth weight, weight on admission, Coombs’ test results, hematocrit level, length of hospital stay and total bilirubin level. However, there was a significant difference between the two groups regarding reticulocyte count.

Conclusion: Based on the findings, establishment of an early G6PD screening program, which can prevent further complications in neonates, seems essential, particularly in countries such as Iran where G6PD deficiency is highly prevalent.

Keywords: Glucose-6-phosphate dehydrogenase, Hyperbilirubinemia, Neonate

Introduction

Jaundice is a commonly reported condition in neonates. Approximately 60% of term and 80% of preterm neonates become icteric in the first week of life. Although jaundice is mostly a physiological phenomenon, it necessitates admission and treatment in 10-12% of cases (1). In severe cases, jaundice can cause complications such as kernicterus, cerebral palsy and death. Consequently, determining the etiology of jaundice can lead to timely prevention and treatment of jaundice (1, 2).

One of the known causes of neonatal jaundice is G6PD deficiency. G6PD is a vital protective enzyme present in all body cells (2, 3). This type of deficiency is the most common and important enzyme deficiency in red blood cells. Lack of G6PD might cause severe hyperbilirubinemia and increase the risk of kernicterus in neonates.

Today, due to appropriate screening of ABO/Rh incompatibility, kernicterus is not normally accompanied by simultaneous blood group incompatibility; therefore, risk of complications has increased in neonates with G6PD deficiency. In previous research, the prevalence of kernicterus was estimated at 6.8% in G6PD deficient infants and 2% in healthy subjects (4).

G6PD deficiency was initially described in 1956. So far, researchers have conducted various studies on this subject (5, 6). At least 400 different types of G6PD deficiency with distinctive biochemical characteristics and about 100 various mutations have been recognized (7).

G6PD deficiency is a hereditary X-linked condition, with a male predominance. Jaundice arising from this deficiency manifests as indirect hyperbilirubinemia. In some studies, the
prevalence of indirect hyperbilirubinemia resulting from G6PD deficiency has been reported to be 7.5% (8). In most cases of hyperbilirubinemia caused by G6PD deficiency, there is no definite finding compatible with hemolysis such as anemia or reticulocytosis.

In some studies, a significant correlation has been reported between G6PD deficiency and Gilbert's syndrome (9). Considering the importance of jaundice resulting from G6PD deficiency and lack of research on this issue, we aimed to determine the prevalence of G6PD deficiency in icteric neonates born in Shirvan, Iran. The incidence rate of G6PD deficiency ranges between 1% and 12% in Asian countries (10).

In this study, we also compared the mean bilirubin level, length of hospital stay, duration of phototherapy, weight loss, exchange transfusion, audometry test and other abnormal, jaundice-related laboratory test results between the two groups with and without G6PD deficiency (case and control groups, respectively). Considering the high prevalence of jaundice and the significant difference in the obtained data between the two groups, we could indicate the necessity of G6PD screening tests for all newborns in Shirvan, Iran.

**Method**

In this descriptive, analytical study, the medical records of neonates, admitted due to jaundice to the neonatal ward of Imam Khomeini Hospital, were evaluated in Shirvan, Iran in 2012-2013. All neonates, who were evaluated in terms of G6PD, were included in our study. Imam Khomeini Hospital of Shirvan is a 120-bed, public hospital. The neonatal ward of this hospital is equipped with 15 beds.

Data of all icteric neonates including the clinical signs and symptoms, laboratory test results and maternal history during pregnancy and childbirth were recorded in the questionnaires by a neonatologist. Maternal history of problems during pregnancy and childbirth, maternal age, maternal infections, mode of delivery, length of hospital stay in mothers after childbirth, gravidity, maternal blood group and follow-up recommendations for the neonates were recorded.

All laboratory tests for evaluating the cause and severity of jaundice including hematocrit level, direct and indirect bilirubin levels, direct and indirect Coombs' test results, reticulocyte count, maternal and neonatal blood groups, thyroid function tests and G6PD were recorded. The patients were divided into two groups with and without G6PD deficiency (case and control groups, respectively). Clinical signs and symptoms, as well as lab test results, were compared between the two groups.

For statistical analysis, data were entered to SPSS version 11.5. For comparing the mean values, standard deviation and the relationship between variables, t-test, Mann-Whitney and Chi-square test were applied. P-value less than 0.05 was considered statistically significant.

**Results**

Overall, 452 cases admitted to the hospital due to jaundice were included in the present study. In total, 16 (3.5%) infants had G6PD deficiency, among whom 13 cases (81.25%) were male and 3 cases (18.75%) were female (Figure 1). In the control group, 248 cases (54.8%) were male and 204 cases (45.2%) were female. According to Chi-square test results, there was a significant association between gender and G6PD deficiency (P=0.000) (Figure 2).

**Figure 1.** Frequency chart of G6PD deficient and sufficient neonates in our study
According to t-test results, there was no significant difference between the case and control groups in terms of variables such as birth weight, weight on admission, Coombs' test results, hematocrit level, length of hospital stay and total bilirubin level. However, there was a significant difference between the two groups regarding reticulocyte count (Figure 3).

In this study, no correlation was found between G6PD deficiency and variables such as mode of delivery, neonatal and maternal Rh blood group or pregnancy-related problems. None of the neonates with G6PD deficiency required exchange transfusion, except for two icteric neonates with normal G6PD. No correlation was detected between exchange transfusion and G6PD deficiency, based on Chi-square test results (P=0.952).

In the present study, the prevalence of G6PD deficiency was estimated at 3.5%. The prevalence of G6PD deficiency in neonates with indirect hyperbilirubinemia varies worldwide, from one race to another. Studies performed in different parts of the world have reported various prevalence rates of G6PD deficiency. For instance, the prevalence rates of this disorder in Spain, France and Singapore were reported to be 1.57%, 2.1% and 1.62%, respectively (11-13), which is considerably low.

In some other world regions such as Saudi Arabia, Nigeria and American Caucasian regions, prevalence of G6PD deficiency has been reported to be high (18%, 40% and 14%, respectively) (14-16). In Iran, G6PD deficiency has a high prevalence rate in some areas including the northern regions, while much lower rates have been reported in other parts including Mashhad (3.7%) and Isfahan (7.5%) (17,18).

In some studies, the correlation between race and G6PD deficiency has been evaluated. For instance, Flyme and Washington in USA showed the higher prevalence of G6PD deficiency in blacks, compared to whites (16, 19). In the present study, there was a significant correlation between gender and G6PD deficiency.

The results reported in some other studies by Boskabadi in Mashhad and Atay in Turkey were consistent with our findings (20, 21).

In the current study, total bilirubin level in the G6PD deficient group was slightly higher than the normal G6PD group. However, the difference was not statistically significant (P=0.203), which was similar to the findings reported by Verma in India (22); this difference should not be attributed to G6PD deficiency.

In the present study, a significant difference was detected in reticulocyte count between the two groups with and without G6PD deficiency (P=0.008); this finding was similar to the results reported by Boskabadi in Mashhad, Iran (21). In our study, no significant difference was noted regarding birth weight, weight on admission, Coombs’ test results or hematocrit level between the two groups. Length of hospital stay was not significantly different between the two groups, which was in accordance with Atay’s findings (20).

Discussion

G6PD deficiency is an X-linked recessive condition. This deficiency makes red blood cells hypersensitive to exposure to oxidants, leading to various clinical manifestations such as neonatal jaundice and hemolytic anemia when exposed to certain foods like fava beans (favism) (1, 2).

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Conclusion

G6PD enzyme deficiency was quite common (3.5%) among neonates, admitted to the hospital due to jaundice. This deficiency can cause
malignant hyperbilirubinemia, which might lead to kernicterus if not diagnosed and treated promptly. Statistically, there was no significant difference between the two groups with and without G6PD deficiency in terms of total bilirubin level, Coombs’ test results, hematocrit level or length of hospital stay, whereas a significant difference was found regarding reticulocyte count. Therefore, establishment of an early G6PD screening program for neonates seems essential in countries such as Iran where the prevalence of G6PD deficiency is high. Such programs are required to prevent subsequent complications by timely diagnosis and treatment.

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References