THE ASSOCIATION BETWEEN G6PD DEFICIENCY AND TOTAL SERUM BILIRUBIN LEVEL IN ICTERIC NEONATES

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Abstract- Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most important disease of the hexose monophosphate pathway. Deficiency of this enzym can lead to hemolysis of red blood cells. Our aim was to study the prevalence of G6PD deficiency in relation to neonatal jaundice. We studied 456 clinically icteric neonates Laboratory investigations included determination of direct and indirect serum bilirubin concentrations, blood group typing, direct coomb's test, hemoglobin, blood smear, reticulocyte count and G6PD level. We divided these neonates to 3 groups based on total serum bilirubin level (TSB): TSB< 20 mg%, TSB=20-25 mg%, and TSB>25 mg%. In only 35 (7.6%) of cases G6PD deficiency was diagnosed. All of these babies were male. From 456 icteric neonates, 213 cases belong to group 1 (TSB<20 mg%), 158 cases belong to group 2 (TSB=20-25 mg%) and 85 cases belong to group 3 (TSB>25 mg%). 16 neonates from 213 neonates of group 1, 6 neonates from 158 neonates of group 2 and 13 neonates from 85 neonates of group 3 had G6PD deficiency. There was statistically significant difference of prevalence of G6PD deficiency between group 2 and 3 (15.3% vs 3.8%)(P = 0.001). Between groups 1 vs 2 and 1 vs 3 no statistically significant difference was found. Early detection of this enzymopathy regardless of sex and close surveillance of the affected newborns may be important in reducing the risk of severe hyperbilirubinemia. This emphasizes the necessity of neonatal screening on cord blood samples for G6PD deficiency.

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Key words: G6PDD, Hyperbilirubinemia, Favism, Neonate

INTRODUCTION

Glucose-6-phosphate-dehydrogenase (G6PD) deficiency is the most common disease-producing enzymopathy in humans. Inherited as an X- linked disorder, G6PD deficiency affects 400 million people worldwide. The disease is highly polymorphic, with more than 300 reported variants.Most patients are asymptomatic. Some patients present with or report a history of neonatal jaundice, often requiring exchange transfusion. Our purpose in this study was determination of prevalence of G6PD deficiency in neonates with different total serum bilirubin levels. In fact, we think that the screening of this enzymopathy is important and necessary in icteric neonates especially cases who referred with total serum bilirubin level above 20 mg/dl.

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MATERIALS AND METHODS

Patient Inclusion Criteria

All of icteric neonates who were admitted to Children's Medical Center in Tehran, Iran, from March 2002 to April 2005. We obtained informed consent from parents of all participents.

Patient Exclusion Criteria

There were no exclusion criteria in this study.

Study Design

In our study, 456 neonates (age: 1-28 days) was evaluated. History taking and Physical examination was performed. Also CBC, PBS, Retic count, direct Coomb's test, total and direct bilirubin level and G6PD was performed for all of these neonates. Also based on total serum bilirubin level, these neonates divided to three groups: group 1 (TSB < 20 mg/dl), group 2 (TSB = 20-25 mg%) and group 3 (TSB > 25 mg/dl).

These data was entered to computer with SPSS statistical program. We used Chi-square analysis method for evaluation of statistically significancy. Confidence interval was 95%.

RESULTS

In only 35 (7.6%) of cases G6PD deficiency was diagnosed. From these, 16 cases (7.5%) were in group 1, 6 cases (3.8%) were in group 2 and 13 cases (15.3%) were in group 3 (Table 1).

There was statistically significant difference of prevalence of G6PD deficiency between group 2 and 3 (15.3% vs. 3.8%) (P = 0.001). Between groups 1 vs. 2 and 1 vs. 3 no statistically significant difference was found (P = 0.1).

Table 1. Prevalence of G6PD in mild, moderate, and severe hyperbilirubinemia*

Group	All	G6PD def.
TSB<20 mg/dl	213 (46.7%)	16 (7.5 %)
TSB = 20-25 mg/dl	158 (34.6%)	6 (3.8 %)
TSB>25 mg/dl	85 (18.7%)	13 (15.3 %)

Abbreviation: TSB, total serum bilirubin level.
* Data are given as number (percent).

DISCUSSION

The etiological relationship between G6PD deficiency and neonatal hyperbilirubinemia has been confirmed by several studies. G6PD-deficient babies are 3-fold more prone to neonatal jaundice than G6PD-deficient infants (1, 2). Most G6PD-deficient individuals are entirely asymptomatic and develop symptoms.

Only in response to oxidant stress. G6PD deficiency does not affect the life expectancy. Of affected individuals. The most common clinical manifestations are neonatal jaundice and acute hemolytic anemia related to drugs, infection or the ingestion of fava beans.

G6PD deficiency is the most common red cell enzymopathy to cause neonatal hemolysis and jaundice. Good population data are available from West Africa (3), the Mediterranean (4) and the Far East (5) and it is clear that perhaps as many as one-third of All males with neonatal jaundice have G6PD deficiency, a similar proportion of male children with G6PD deficiency developing neonatal jaundice (NNJ). Early observations suggested that the incidence of NNJ was significantly lower among subjects of African Ancestry in the USA than in Africa, suggesting that environmental as well as genetic factors in uence expression. It is, however, clear that all subjects with G6PD are at increased risk of NNJ (6), and kernicterus has been reported in all at-risk population groups. Public health programs have significantly reduced the incidence of kernicterus in some parts of the world [*e.g.* Singapore (7)] but not others [*e.g.* Pakistan (8)]. Environmental and cultural factors that in-uence the incidence of NNJ Include maternal exposure to oxidant drugs, the use of herbal remedies, and the incidence of neonatal infection, hypoglycemia and acidosis, and the normal level of neonatal Hemoglobin within a population. It has long been assumed that these factors combine with an increased susceptibility of neonatal erythrocytes to hemolysis to give rise to an increased incidence and extent of hemolysis.

However, recent evidence suggests that hemolysis is only partly responsible, decreased bilirubin conjugation and elimination playing a

major role in the pathogenesis of NNJ (9). The presence of an additional hemolytic process such as ABO incompatibility was found to have little impact on the degree of hemolysis and hyperbilirubinemia (10). These observations confirm those first made in Sardinia, where the severity of NNJ does not correlate with red cell G6PD activity (11), that the hyperbilirubinemia is largely the result of an impairment of liver function caused by G6PD deficiency in the liver (12).

According to a WHO report, Iran is in a moderately high incidence area for G6PD deficiency (13). Favism is also common in some provinces of Iran, the objectives of this study were to estimate the incidence of G6PD deficiency in newborns of Tehran (capital of Iran) and to establish its relationship with hyperbilirubinemia.

In our study, there was statistically significant difference between the prevalence of G6PD deficiency and total serum bilirubin level (compared group 2 and 3) ($P = 0.001$). It seems that, in severe hyperbilirubinemia (TSB > 25 mg/dl) the prevalence of G6PD deficiency is more than moderate hyperbilirubinemia (TSB = 20-25 mg/dl) that may be a risk factor for some complications as kernicterus.

Conflict of interests

The authors declare that they have no competing interests.

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