

FREQUENCY OF G6PD DEFICIENCY IN NEONATAL HYPERBILIRUBINEMIA

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ABSTRACT

Background: Glucose-6-phosphate dehydrogenase is the commonest enzymopathy in human beings. Acute hemolytic crisis is the most common presentation of G6PD deficiency but in neonatal period it usually presents as jaundice. The objective of this study is to determine the frequency of G6PD deficiency in jaundiced neonates.

Material & Methods: This study was conducted at Children Hospital, Pakistan Institute of Medical Sciences, Islamabad from 27th March 2009 to 27th September 2009. One hundred and sixty-three jaundiced neonates were included. Screening for G6PD deficiency was done by dye decolorization test, which is semi quantitative, visual colorimetric assay.

Results: The study included 163 neonates with jaundice. 72.4% were males and 27.6% were females. 16% were pre-term and 84% were full term babies. The mean age was 4.77 ± 2.80 days. 11 (6.7%) were G6PD deficient. 46% were anemic. Maturity at birth, time of presentation, presence of anemia and hyperbilirubinemia and reticulocytosis were not significantly different between G6PD deficient and G6PD normal neonates.

Conclusion: Frequency of G6PD deficiency is higher in neonatal hyperbilirubinemia. G6PD assay should be included in all jaundiced neonates for earlier detection and timely prevention of complication like kernicterus.

KEY WORDS: Neonates; Jaundice; G6PD deficiency.

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INTRODUCTION

Glucose 6-phosphate dehydrogenase (G6PD) deficiency, an X-linked disorder, is the most common enzymatic disorder of red blood cells in humans, affecting more than 400 million people worldwide.¹ About 60% of term babies and 80% of pre-term infants develop some degree of jaundice during their first week of life.² But, the jaundice due to G6PD deficiency occurs in the 1st day of life and usually severe (pathological) in nature.³ The clinical expression of G6PD variants encompasses a spectrum of hemolytic syndromes. Affected patients are usually asymptomatic but many patients have episodic anemia while a few have chronic hemolysis.

With the most prevalent G6PD variants (G6PD A- and G6PD Mediterranean), hemolysis is induced in children and adults by the sudden destruction of older, more deficient erythrocytes after exposure to drugs having a high redox potential (including the

antimalarial drug primaquine and certain sulfa drugs like sulfanilamide, sulfamethoxazole, mafenideor) or to fava beans, selected infections, or metabolic abnormalities. However, in the neonate with G6PD deficiency, decreased bilirubin elimination may play an important role in the development of jaundice.^{4, 5}

Although G6PD deficiency is global in its distribution, it occurs most often in the tropical and subtropical zones of the Eastern Hemisphere. As examples, G6PD deficiency is present in approximately 20 percent of African Bantu males, 8 percent in Brazilian blacks, 20 to 35 percent in the lowlands of Sardinia and Greece (with a much lower prevalence at higher altitudes), as high as 60 to 70 percent in Kurdish Jews, and in Asia, 5.5 percent in South China, 2.6 percent in India and less than 0.1 percent in Japan.⁶⁻¹²

In the United States, G6PD deficiency is present in about 12 percent in African-American men. In addition as many as 20 percent of African-American women are heterozygous for G6PD mutants and as many as 1 percent are homozygous. G6PD deficiency is rare among Native Americans.¹³⁻¹⁶

The objective of this study is to determine the

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frequency of G6PD deficiency in jaundiced neonates.

MATERIAL AND METHODS

This study was conducted at Children Hospital, Pakistan Institute of Medical Sciences, Islamabad from 27th March 2009 to 27th September 2009.

One hundred and sixty-three jaundiced neonates were included in the study. Screening for G6PD deficiency was done by dye decolorization test, which is semi quantitative, visual colorimetric assay. Those having congenital defect, autoimmune hemolysis, in moribund condition low APGAR (Appearance, Pulse, Grimace, Activity, Respiration) score, acute hemolysis characterized by reticulocytosis and established maternal positive status for hepatitis B and C virus were excluded from study. All the patients meeting the inclusion criteria from all incoming sources to hospital like outpatient department, Emergency department and hospitalized patients were included. Approval was taken from hospital ethical committee. Informed written consent was taken from the parents/ caretakers. Blood samples were taken for blood complete picture (CP), G6PD test and serum bilirubin level. Screening for G6PD deficiency was done by the dichlorophenol-indophenol (DPIP) dye decolorization method (Bernstein 1962).¹⁷ Bilirubin was measured by the Van Den Bergh method.¹⁸ Hematological parameters were measured using an automatic hematology analyzer (Nihon Khoden) as per the manufacturers' instructions.

The data was analyzed using SPSS version 12. Mean and standard deviation were calculated for numerical variables like, age, bilirubin, reticulocytes count and hemoglobin levels. Frequencies were represented for categorical variables i.e. age, gender, preterm, full term and G6PD deficiency.

RESULTS

The study included 163 neonates with jaundice. 118 (72.4%) were males and 45 (27.6%) were females. 26 (16%) were preterm and 137 (84%) were full term babies. The mean age was 4.77 ± 2.80 days. The age ranged from 1 to 17 days. 11 (6.7%) were G6PD deficient. 152 (93.3%) had normal G6PD levels. 22 (13.5%) presented within the first 24-hour after birth, 112 (68.7%) presented between 2-7 days and 29 (17.8%) presented after the first week of birth. 75 (46%) were anemic with a hemoglobin less than the reference value for their age. The hemoglobin ranged from 7 to 20 g/dl with a mean of 15.43 ± 2.81 g/dl. The total bilirubin ranged from 6.3 to 36 mg/dl with a mean of 18.98 ± 6.20 mg/dl. The direct bilirubin ranged from 0.5 to 22.5 mg/dl with a mean of 2.40 ± 1.94 mg/dl. The indirect bilirubin ranged from 0.90 to 32 mg/dl with a mean of 16.32 ± 6.31 mg/dl. The retics count ranged from 0.4 to 25% with a mean of 4.11 ± 4.1 .

Table 1: Characteristics of patients with hyperbilirubinemia (n=163).

	G6PD deficient	Non-G6PD deficient
Total number	11	152
Preterm	3/11	23/152
Full term	8/11	129/152
Mean Age (Days)	5.3 ± 1.36	4.7 ± 2.88
Mean Hb (g/dl)	14.7 ± 2.84	15.4 ± 2.81
Anemia	7/11 (63.6%)	68/152
Mean Total Bilirubin (mg/dl)	22.23 ± 7.65	18.75 ± 6.05
Mean Retic count (%)	2.94 ± 1.86	4.19 ± 4.29
Mean direct bilirubin (mg/dl)	3.09 ± 2.03	2.35 ± 1.93
Mean indirect bilirubin (mg/dl)	19.9 ± 6.68	16.08 ± 6.24

Among the 11 G6PD deficient neonates, 10 were males and one female. Among 152 non-G6PD deficient neonates, 108 were males and 44 females. ($p=0.15$). Among G6PD deficient neonates 1/11 (9.1%) had total bilirubin <20 mg/dl, 4/11 (36.4%) had bilirubin between 20-30 mg/dl and 6/11 (54.5%) had bilirubin >30 mg/dl. Among normal G6PD neonates 23/152 (15.1%) had total bilirubin <20 mg/dl, 73/152 (48%) had bilirubin between 20-30 mg/dl and 56/152 (36.8%) had bilirubin >30 mg/dl; this difference was not statistically significant. ($p=0.49$)

DISCUSSION

G6PD deficiency is the most important disease of hexose monophosphate pathway. G6PD is an x-linked recessive disease, where the deficiency of the enzyme causes a spectrum of clinical manifestations ranging from neonatal jaundice to chronic nonspherocytic anemia, to infection and drug-induced hemolysis.¹⁹

Local data on the subject is scarce. Siddiqi et al reported G6PD deficiency in 5.4% of neonates with jaundice; these results were in conformation with our study.²⁰ In a study by Alvi et al,²¹ 10% of the neonates with pathological hyperbilirubinemia were found to be G6PD deficient. Rehman et al²² reported that 8.2% babies admitted for neonatal jaundice were G6PD deficient. In another study from Peshawar, Imran et al found that 11.2% of the neonates admitted for neonatal jaundice were G6PD deficient.²³ This difference could be due to the different incidence of G6PD deficiency in different parts of the world, and

ethnic groups, within the same country.

At Khyber Teaching Hospital Peshawar in 2003 out of 200 adult patients studied, 24 (12%) patients were found to be deficient in G6PD enzyme.²⁴ In our study we detected a male to female ratio of 10: 1. So the number of girls with G6PD deficiency should not be underestimated.

Hyperbilirubinemia in G6PD-deficient neonates is thought to be secondary to reduced hepatic conjugation and excretion of bilirubin, rather than increased bilirubin production resulting from hemolysis. In our study we found no difference in reticulocyte count and hemoglobin level between G6PD-deficient and normal groups. In our study among G-6-PD deficient neonates 1/11 (9.1%) has total bilirubin < 20 mg/dl, 4/11 (36.4%) had bilirubin between 20-30 mg/dl and 6/11 (54.5%) had bilirubin > 30 mg/dl. Among normal G-6- PD neonates 23/152 (15.1%) has total bilirubin < 20 mg/dl, 73/152 (48%) had bilirubin between 20-30 mg/dl and 56/152 (36.8%) had bilirubin > 30 mg/dl.; of the G6PD deficient neonates had a peak serum bilirubin > 20 mg/dl. .

Our results were consistent with study by Alvi et al²¹ in which 90% neonates developed jaundice within first 7 days of life and also with the study from Peshawar in which 80% babies with G6PD deficiency developed jaundice in first 7 days of life. This difference was not statistically significant ($p=0.498$). Evidence of hemolysis was lacking in most of the G6PD deficient babies in our study, as reticulocytes was not evident in most of the G6PD deficient neonates in our study. G6PD deficiency associated with neonatal jaundice was considered to be hemolytic in origin, but a number of studies have proven that hemolysis is not the only reason for jaundice in these. It is now considered predominantly to be caused by G6PD deficiency being expressed in the liver, resulting in partial defect of bilirubin conjugation and its decreased excretion. More studies on a larger scale are required to document the prevalence of G6PD among jaundiced neonates in different regions and races of Pakistan

CONCLUSION

Frequency of G6PD deficiency is higher in neonatal hyperbilirubinemia. G6PD assay should be included in all jaundiced neonates for earlier detection and timely prevention of complications like kernicterus.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

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None declared.