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Glucose-6-Phosphate Dehydrogenase Deficiency in Neonatal Hyperbilirubinemia

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Abstract

Background: The Glucose-6-phosphate dehydrogenase (G6PD) deficiency has been considered as the commonest enzymopathy inherited disorder of red blood cells, which affecting more than 400 million people worldwide. To study the Glucose-6-phosphate dehydrogenase (G6PD) deficiency in neonatal hyperbilirubinemia

Methods: The study was carried out at the Department of Pathology, Jhalawar Medical College Jhalawar, and the neonatal intensive Care Unit (NICU) of department of Pediatrics SHKB Hospital Rajasthan. It is a tertiary care hospital and teaching institute .This serve as referral Centers for the Jhalawar city as well as the neighboring villages of Jhalawar district. Admissions into the NICU are commonly for perinatal asphyxia, neonatal sepsis, neonatal jaundice, and prematurity.

Results- Out of 7 subjects with G6PD deficiency, 4 were with >2500gm birth weight and 3 with <2500gm birth weight. Out of 374, 140 G6PD normal patients were with <2500gm birth weight and 234 were with >2500gm. Similar findings were observed for weight at presentation. G6PD deficient and normal patients have different hemoglobin concentration being 14.1143±4.12 and 14.7±4.05 respectively. PCV levels were observed to be 44.7286±8.09 and 46.2620±19.61 respectively. G6PD deficient has lower reticulocyte count than normal. It was found to be 7.37±2.01and 2.33±1.00 respectively

Conclusion: We conclude that G6PD deficiency is a common enzyme defect in our neonatal population (especially male) causing severe indirect hyperbilirubinemia requiring treatment; however, a larger study is required to validate the same. Early neonatal screening programs should be instituted to anticipate and institute early treatment to prevent morbidity and mortality

Keywords: G6PD deficiency, Neonatal hyperbilirubinemia, NADPH.

Introduction

The Glucose-6-phosphate dehydrogenase (G6PD) deficiency has been considered as the commonest

enzymopathy inherited disorder of red blood cells, which affecting more than 400 million people worldwide.[1]

Neonatal hyperbilirubinemia (defined as a total serum bilirubin level exceeding 5 mg/dl) is a frequent problem as neonatal jaundice affects 65% of full-term infants and 85% of preterm infants after 24 h of life.[2]

The glucose-6-phosphate dehydrogenase (G6PD) enzyme is part of the pentose monophosphate shunt. It catalyzes the oxidation of glucose-6-phosphate and the reduction of nicotinamide adenine dinucleotide phosphate to nicotinamide adenine dinucleotide phosphate (NADPH). NADPH maintains glutathione in its reduced form, which acts as a scavenger for dangerous oxidative metabolites. The erythrocytes do not generate NADPH in any other way; they are more susceptible than other cells to destruction from oxidative stress. The most common clinical feature of G6PD deficiency is a lack of symptoms. However, in symptomatic neonates, the presenting features are neonatal jaundice and/or acute hemolytic anemia.

Jaundice usually appears by age 1–4 days, at the same time as or slightly earlier than physiological jaundice. The prevalence of neonatal hyperbilirubinemia is twice that of the general population in males who carry the defective gene and in homozygous females. It rarely occurs in heterozygous females.[3] Infants with the severe variant of G6PD deficiency may develop severe hyperbilirubinemia to cause kernicterus.

Materials And Methods

Study Area: The study was carried out at the Department of Pathology, Jhalawar Medical College Jhalawar, and the neonatal intensive Care Unit (NICU) of department of Pediatrics SHKB Hospital Rajasthan. It is a tertiary care hospital and teaching institute .This serve as referral Centers for the Jhalawar city as well as the neighboring villages of Jhalawar district. Admissions into the NICU are commonly for perinatal asphyxia, neonatal sepsis, neonatal jaundice, and prematurity.

Inclusion Criteria

New born with the following criteria will be included:

1. Serum bilirubin>15mg/dl.
2. Jaundice appearing within 24 hours of birth.
3. Cord blood serum bilirubin >5 mg /dl.
4. Jaundice lasting>10days in full term and>14days in preterm babies.

Exclusion Criteria

1. Physiological jaundice in term and preterm babies.
2. Congenital anomalies.
3. Polycythemia, Cephalohematoma, ABO incompatibility, Sepsis, Infant of diabetic mother.

Method of data collection

Neonates in department of Paediatrics Jhalawar medical college, Jhalawar (Rajasthan) are included in the study. Consent was obtained from the parent or parents of each neonate. A standardized questionnaire (Performa-appendix 3) was utilized for the parent or parents of the neonate to obtain relevant demographic, social, and medical history. The Performa consisted of two sections: A and B with section A for bio-data, maternal history, neonatal history and physical examination while Section B consists of laboratory investigations. The researcher filled the questionnaire addressing parameters such as age, weight of the patient and estimated gestational age.

The neonates were examined (general and systemic) by the pediatricians. Blood samples were then collected from the neonates for complete blood count (CBC), reticulocyte count, antihuman globulin test, G6PD

enzyme assay(qualitative) and quantitative assay in selected cases, ABO and Rh blood grouping. Mothers' blood sample was also collected for her ABO and Rh blood grouping.

Statistical analysis

The data collected was analyzed using SPS software. Mean, median, and standard deviation (SD) were used to describe continuous data.. Chi-square was used to compare categorical data. P-value of less than 0.05 was considered statistically significant. The results were reported in tables, proportions, and percentages.

Results

Table1: Clinical and Laboratory parameters of all subjects and G6PD status

S.NO	Parameters		G6PD deficient(n=7)	G6PD normal(n=383)	p-value
1	Age (days)		4.57±4.39	3.10±1.92	>0.05(NS)
2	Sex	Male	5	241	<0.05(Sig)
		Female	2	142	
3	Duration of pregnancy	Full term	4	278	<0.05(sig)
		Pre term	3	105	
4	Age at presentation		3.42±4.46	2.15±1.93	>0.05(NS)
5	History of jaundice in siblings		0	43	<0.05(sig)
6	Weight at birth	<2500gm	3	140	<0.05(sig)
		>2500gm	4	234	
7	Weight at presentation	<2500gm	3	140	<0.05(sig)
		>2500gm	4	234	
8	Hemoglobin concentration(gm/dl)		14.11±4.12	14.7±4.05	>0.05(NS)
9	PCV (%)		44.72±8.09	46.26±19.61	>0.05(NS)
10	Reticulocyte count (%)		7.371±2.01	2.33±1.001	<0.05(sig)
11	TLC(103/ul)		9140±280.91	9557.95±281.87	<0.05(sig)
12	Platelet count(103/ul)		291.57±98.76	222.657±101.71	<0.05(sig)

Out of 7 subjects with G6PD deficiency, 4 were with >2500gm birth weight and 3 with <2500gm birth weight. Out of 374, 140 G6PD normal patients were with <2500gm birth weight and 234 were with >2500gm. Similar findings were observed for weight at presentation. G6PD deficient and normal patients have different hemoglobin concentration being 14.1143±4.12 and 14.7±4.05 respectively. PCV levels were observed to be 44.7286±8.09 and 46.2620±19.61 respectively. G6PD deficient has lower reticulocyte count than normal. It was found to be 7.37±2.01and 2.33±1.00 respectively

Table 2: G6PD status and severity of hyperbilirubinemia

Degree of Hyperbilirubinemia	Deficient			Normal			P-Value
	N	%	Mean SB	N	%	Mean SB	
Mild	2	28.57	18	264	68.93	16.75	<0.05(Sig)
Moderate	2	28.57	23.6	104	27.15	22.13	>0.05 (Non Sig)
Severe	3	42.86	28.77	15	3.92	26.85	<0.05(Sig)

Severe degree of hyperbilirubinemia was found in 42.86% of patients with G6PD deficiency, whereas 68.93% patients showed mild degree of hyperbilirubinemia in G6PD normal patients.

Discussion

The present prospective study was conducted in the Department of Pathology, Jhalawar Medical College, Jhalawar (Rajasthan), India. Neonates with hyperbilirubinemia during 1.5 years period from June2019 to November 2020, admitted to the Department of pediatrics were included in the study after properly stratifying according to inclusion and exclusion criteria.

G6PD is one of the antioxidant enzymes that protect the cell from injury. [(4)] G6PD deficiency is an X-linked recessive disorder, the most common enzyme deficiency worldwide, affecting around 400 million people. It can cause a spectrum of disease including neonatal hyperbilirubinemia, acute hemolysis, and chronic hemolysis. The gene that codes for G6PD is located in the distal long arm of the X chromosome at the Xq28 locus. The G6PD gene is 18 kb long with 13 exons, and the G6PD enzyme has 515 amino acids. More than 60 mutations in the G6PD gene have been documented. The World Health Organization has classified the different G6PD variants according to the degree of enzyme deficiency and severity of hemolysis, into Classes I-V. Class I deficiencies are the most severe. G6PD Mediterranean deficiency usually is a Class II deficiency and G6PD A deficiency is a Class III deficiency. Classes IV and V are of no clinical significance. It has been reported that one-third of children with G6PD deficiency develop neonatal jaundice. [5]

G6PD deficiency is estimated to affect 400 million individuals worldwide. It is more common in the Mediterranean area, Middle East, India, China, and Africa. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a hereditary condition resulting from a structural defect in G6PD, a "housekeeping" enzyme that is particularly important for the survival of red blood cells and their ability to respond to oxidative stress. G6PD deficiency is an independent risk factor for high serum bilirubin level ≥18 mg/dL. It is considered as one of the most common clinically significant enzyme defects.[6] Glucose 6-phosphate dehydrogenase (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. G6PD-deficient individuals are usually healthy and asymptomatic but acute hemolysis may occur after ingestions of certain drugs, food, and exposure to certain chemicals, infections or hypoxia. They could be attributable to the early onset hemolysis due to oxidative stress as a result of perinatal events.

The glucose-6-phosphate dehydrogenase (G6PD) enzyme is part of the pentose monophosphate shunt. It catalyzes the oxidation of glucose-6-phosphate and the reduction of nicotinamide adenine dinucleotide phosphate to nicotinamide adenine dinucleotide phosphate (NADPH). NADPH maintains glutathione in its reduced form, which acts as a scavenger for dangerous oxidative metabolites. The erythrocytes do not generate NADPH in any other way; they are more susceptible than other cells to destruction from oxidative stress. The most common clinical feature of G6PD deficiency is a lack of symptoms. However, in symptomatic neonates, the presenting features are neonatal jaundice and/or acute hemolytic anemia. Jaundice usually appears by age 1–4 days, at the same time as or slightly earlier than physiological jaundice.[7-8]

Conclusion

We conclude that G6PD deficiency is a common enzyme defect in our neonatal population (especially male) causing severe indirect hyperbilirubinemia requiring treatment; however, a larger study is required to validate the same. Early neonatal screening programs should be instituted to anticipate and institute early treatment to prevent morbidity and mortality.

References

1. Mehta A, Mason PJ, Vulliamy TJ. (2000): Glucose-6-phosphate dehydrogenase deficiency. Best Prac Res Clin aematol, 13: 21-38.
2. Prchal JT, Gregg XT (2005): Red Cell Enzymes. Hematol, 1:19-23.
3. Mason PJ, Bautista JM, and Gilsanz F, (2007): G6PD deficiency: the genotypephenotype association. Blood Rev 21 267-83.
4. Groenendaal F, der Grond JV, De Vries LS (2004). Cerebral Metabolism in Severe Neonatal Hyperbilirubinemia. Pediatr, 114: 291-94.
5. Kaplan M, Muraca M, Hammerman C, Vilei MT, Leiter C, Rudensky B, et al. (1998). Bilirubin Conjugation, Reflected by Conjugated Bilirubin Fractions, in Glucose-6-PhosphateDehydrogenase-deficient Neonates: A Determining Factor in the Pathogenesis of Hyperbilirubinemia. Pediatr, 102 (3): e37.
6. Zahed Pasha A, Ahmadpoor M, Zahed Pasha Y (2006). Glucose-6-phosphate dehydrogenase Enzyme Deficiency. J Babol Univ Med Sci, 8(1).
7. Markić J, Krželj V, Markotić A, Marušić E, Stričević L, Zanchi J, et al. (2006). High Incidence of Glucose-6-phosphate Dehydrogenase Deficiency in Croatian Island Isolate: Example from Vis Island, Croatia. Croat Med J, 47: 566-70.
8. Frank EJ (2005). Diagnosis and Management of G6PD Deficiency. Am family phys, 72: 1277-82.