FREQUENCY OF G6PD DEFICIENCY AND ITS SEVERITY IN NEONATAL JAUNDICE IN REHMAN MEDICAL INSTITUTE, PESHAWAR

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ABSTRACT

Objective: To detect the frequency of glucose 6-phosphate dehydrogenase (G6PD) and its association with neonatal jaundice.

Methodology: This hospital based comparative study was conducted on neonates admitted for neonatal jaundice at Rehman Medical Institute Peshawar, Pakistan from 1st Jan, 2006 to 1 June, 2012. A total of 4900 patients were admitted during this time period, of which 1695 (34.6%) neonates were treated for neonatal Jaundice. Estimation of serum bilirubin (both direct and indirect) was done in all cases and G6PD was done in cases with severe jaundice or with any absolute indication.

Results: Out of the total 1695 patients admitted for neonatal jaundice, 152(9%) babies were found to be G6PD deficient. Majority of the patients presented with jaundice in the first 4 days of life. G6PD was found to be the most severe form of jaundice with 56% out all exchange transfused neonates were having no other risk factor but G6PD deficiency. ABO (31.97%) and sepsis (30%) were the common causes of neonatal jaundice.

Conclusion: G6PD is one of the common causes of neonatal jaundice. Babies with G6PD can present earlier and can have serious consequences.

Key Words: Glucose 6-Phosphate Dehydrogenase, G6PD deficiency, Neonatal Jaundice, Bilirubin.

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INTRODUCTION

The neonatal jaundice can be either physiological or pathological. More than 60% of healthy newborns develop jaundice associated with increased concentration of serum bilirubin during first week of life[1]. The hyperbilirubinaemia usually resolves by 7-10 days of age depending on the underlying condition and the outcome is usually benign (termed as physiological jaundice)[1,2]. Without proper and timely management significant increase in serum bilirubin level to values greater than 25mg/dl can lead to serious complications like brain damage (kernicterus)[2].

Red blood cells are known for their shape, structure, biosynthetic apparatus and stability. The integrity depends upon various enzymes. One of the important enzymes is Glucose-6-phosphate dehydrogenase (G6PD).[3]

The most common etiologies in the majority of neonatal jaundice include: Hemolytic disorders (Rhesus Incompatibility, ABO Incompatibility, intrinsic red blood cell defect etc.), G6PD deficiency, Sepsis, Idiopathic causes (delayed or impaired function of glucoronyl transferase enzyme system), breast feeding jaundice and inadequate nutrition intake.

G6PD deficiencies, is the most common disease producing enzymopathy in humans.[4] Inherited as an X-Linked disorder, so the prevalence of G6PD in any population is determined by the number of deficient males. However deficient females are also at risk of hemolysis and jaundice.[5] G6PD deficiency affects 400 million peoples worldwide.[6] The G6PD gene is located on the long arm of X chromosome.[7] The advances in molecular biology explored the genetics G6PD deficiency with more than 300 reported variants.[7-9] Different mutations cause different level of enzyme deficiency, with various clinical manifestations.[10,11] Some presenting with neonatal jaundice while other present with chronic hemolytic anemia and if not managed on time can also present with kernicterus[7]. Public health programs have significantly reduced the incidence of kernicterus in some parts of the world like Singapore[12] but not in developing countries like Pakistan[13]. Environmental and cultural factors that influence the incidence of neonatal jaundice 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.

Patients present mostly with neonatal jaundice, some of them requiring exchange transfusion. There is considerable evidence to believe that the prevalence of G6PD deficiency in Pakistan is ranging from 2-3.8%, with highest frequency of 8.6% in Pathans.[14] According to Saha et al, presence of 563C-T and silent mutation of 1311C-T is identified as the sole cause of pattern and prevalence of G6PD deficiency in these ethnic groups (Pathans and Punjabis).[15] The aim of our study was to detect the incidence of G6PD deficiency in hyperbilirubinaemic neonates and to determine its severity.

METHODOLOGY

The study was carried out at neonatal intensive care unit (NICU) of Rehman Medical Institute Peshawar, from Jan 2006 - Jun 2012 on all cases admitted for neonatal jaundice; the neonates with indirect hyperbilirubinaemia were included in the study. Detailed history, examination and all the necessary investigations like, complete blood count, blood groups of mother and infant, Coombs' test (Rhesus negative mother), total serum Bilrrubin level (direct/indirect), reticulocytes count and glucose 6 phosphate dehydrogenase deficiency screening test, C-reactive protein and Blood Culture (if sepsis is suspected). The therapy (Phototherapy or exchange therapy) in our setup is started by plotting the child SBR on a monogram[16].

After collecting blood (1.5-2 ml) from a vein under strict hygienic condition, the blood is put into an EDTA tube and then sent to the laboratory for processing where the whole process takes 2-3 hours to get the final report. Qualitative test for glucose 6 phosphate dehydrogenase deficiency was performed, which uses the diagnostic reagent kit for the in vitro determination of the activity of the glucose 6 phosphate dehydrogenase from the red cell hemolysate. G6PD deficiency, present in the red cell hemolysate acts on gluose-6-phosphate and reduces NADP to NADPH which with the help of PMS (Phenazine methosulfate) reduces blue colored 2,6 dichlorophenol indophenol into a colorless form. The rate of decolourization is proportion to the enzyme activity. The advantage of this test is simple, more specific visual method, no need for colorimeter and highly economical. The reagents used are Substrate, buffer (P^h 8.5) and mineral oil.

Decision regarding the treatment was taken on the basis of serum indirect bilirubin level and age of the baby.

RESULTS

A total of 4900 neonates were admitted in the NICU of Rehman Medical Institute, Peshawar for Neonatal jaundice from Jan 2006 to Jun, 2012. These neonates included 1695 (34.6%) cases of neonatal jaundice. Out of these 1695 neonates 152(9%) were having glucose 6 phosphate dehydrogenase deficiency. Other etiologies of hyperbilirubinaemia in these cases are also shown in Table I including ABO incompatibility 542(32%), Sepsis (related Jaundice) 509(30%) and Rhesus Disease 322(19%).

Majority of the neonates with jaundice and G6PD deficiency presented between 2-4 days after birth 136(89.4%) as shown in Table II. While 84 (55%) of the patient with G6PD deficiency presented with severe hyperbillirubenmia with swerum bilirubin (SBR) level of greater than 20 mg/dl.

Table III shows severity of different etiologies depending on the severity of hyperbilirubinaemia, the patient admitted for neonatal jaundice were either given phototherapy or exchange transfusion (in the severe cases), in our this study of the total neonates admitted for neonatal jaundice, 1543 (91.03%) were given phototherapy whereas exchange transfusion was done in 152 (8.97%) of cases. Out of 152 cases of G6PD deficiency, 84 (55.3%) patients were given exchange transfusion and 68 (44.7%) patients were given phototherapy.

DISCUSSION

The association between G6PD deficiency with severe neonatal jaundice and kernicterus was first described in 1960.[17] Neonatal jaundice is one of the major causes of admission to the neonatology unit, it is estimated that 1/4th of all admissions in a Neonatology unit is due to neonatal jaundice; our study shows that 34.6% of the admission were due to neonatal jaundice, the severity of jaundice depends on the underlying etiological factors.

Glucose 6 phosphate dehydrogenase deficiency is one of the major causes of severe hyperbilirubinaemia that if not managed well on time can lead to kernicterus or even death. G6PD deficient babies are 3-fold more prone to neonatal jaundice than those who are normal.[18,19]

In this study, the cause of jaundice could not be determined in 7.8% of cases. Some of these cases were probably due to physiological jaundice, breast feeding jaundice, due to hypothyroidism etc.

In the present study, the frequency of G6PD deficiency among neonates with hyperbilirubinaemia has been found to be 9.8%. This finding of our study is consistent with other studies which reported the incidence of G6PD deficiency as 10.65% in Iraq[20] and 12.6% in Saudi Arabia.[21] In Pakistan, the incidence of G6PD deficiency in neonates was reported as 10% by Alvi et al in 2006[22], 12% by Imran et al,[23] 12.1% by Perveen et al[24] at Lahore and 13% by Khan et al[25]. Khattak et al at Peshawar, observed G6PD deficiency in 12% of patients with hemolytic anaemia.[26]

In contrast to our study, some other studies showed a higher incidence of G6PD deficiency; it has been reported to be 16% in a study done in Peshawar[27], another study done by Fazal Rahim[28], in which he reported the incidence of

TABLE I: ETIOLOGY OF NEONATAL JAUNDICE AND FREQUENCY OF GLUCOSE 6 PHOSPHATE DEHYDROGENASE

Etiology of neonatal jaundice	No. of cases	Percentage
Glucose 6 phosphate dehydrogenase deficiency	152	09
ABO incompatibility	542	32
Sepsis	509	30
Rhesus diseases	322	19
Cephalhematoma	51	03
Misc Causes (Breast feeding Jaundice, Hypothyroidism, etc)	119	07
Total	1695	100

TABLE II: AGE OF PRESENTATION & SERUM BILIRUBIN LEVEL IN PATIENTS WITH NEONATAL JAUNDICE (n=152)

Characteristics		No. of cases (n=152)	Percentage
Age of Presentation	Up to 24 hours	04	2.6%
	2nd Day to 4th day	136	89.4%
	After 4 days	12	8%
Serum Bilirubin (SBR) Level	<20mg%	68	44.7%
	> 20 mg%	84	55.3%

TABLE III: CAUSE VS THERAPY IN DIFFERENT ETIOLOGICAL CAUSES OF NEONATAL JAUNDICE

Causes	Therapy			
	Phototherapy		Exchange Transfusion	
	No. of cases	Percentage	No. of cases	Percentage
G6PD	68	4.45	84	56
ABO	508	32.90	34	22
RHESUS	288	18.67	34	22
Sepsis	509	32.92	—	—
Cephalhematoma	51	3.30	—	—
Misc. (Breast Milk, Hypothyroidism, etc.)	119	7.76	—	—
Total	1543	100	152	100

glucose 6 phosphate dehydrogenase deficiency to be 26% in DHQ Timargara Dir. A study done by Woodfield[29] in Papua New Guinea reported 22%, Al-Namma[18] LM in Basra reported 51%, Dawodu AH from Nigeria[30] reported 62% incidence of G6PD.

G6PD deficiency is a common cause of neonatal jaundice in our study and has been the most severe form of Jaundice as most of the cases were in the range of exchange transfusion. The reason for this might be because of more emphasis on earlier detection and treatment of other causes of neonatal jaundice like Rhesus and ABO incompatibly, also the need for glucose 6 phosphate dehydrogenase deficiency early detection and prompt treatment rises even more as the incidence of G6PD deficiency is relatively high in Pathans[15].

CONCLUSION

Glucose 6 phosphate dehydrogenase deficiency is one of the common causes of neonatal jaundice. The babies suffering from G6PD deficiency can present with jaundice earlier than the other etiologies. In our study, G6PD deficiency was the most severe form of neonatal jaundice as majority of the babies requiring exchange transfusion. From our study we suggest that screening for G6PD deficiency should be included in schedule for neonates who presents with jaundice so as to prevent complications like billirubin encephalopathy.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

AZJ: Conception and design, Acquisition of data, Drafting the manuscript, : final approval of the version to be published

SBZ: Acquisition of data, Analysis and interpretation of data, final approval of the version to be published

SA: Drafting the manuscript, Critical revision, final approval of the version to be published

CONFLICT OF INTEREST

Author declares no conflict of interest

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