NEONATAL HYPERBILIRUBINAEMIA SECONDARY TO ERYTHORCYTE GLUCOSE-6-PHOSPHATE DEHYDROGENEASE DEFICIENCY

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SUMMARY

This study was conducted in the special care baby unit of Khyber Teaching hospital, Peshawar form July 1998 to June 1999. During his period about 200 newborn babies with hyprbilirubinaemia were studied for the etiological causes. All were full term. Their age ranged form 1 to 7 days. Out of these 200 jaundice babies 26(13%) were found to be deficient in G6PD enzyme. The sex ration was M:F 23:3 (88.5% and 11.5%) respectively. Age of appearance of jaundice varied from 1st 24 hours of life upto 5 days (mean 2 ½ days). Mean serum bilirubin level was 18.7mg%. Seventeen (65%) babies developed severe hyperbilirubinaemia (SBR level more than 20mg%) and were given exchange blood transfusion. All of the G6PD deficient babies received phototherapy. Two babies (8%) developed bilirubin encephalopathy. Average hospital stay was 7 days. Phototherapy and exchange blood transfusion are effective in reducing the serum indirect bilirubin levels but once kernicterus develops, no treatment can reverse it. Therefore all jaundiced newborn babies should be screened for G6PD deficiency to reduce the immediate risk of bilirubin encephalopathy and later on of haemolysis.

INTRODUCTION

G6PD deficiency is an x-linked hereditary disorder. This enzymopathy was discovered in 1950 as an outgrowth of studies of the unique sensitivity of some persons to the hemolytic action of certain drugs.[1] Now more than forty different mutations and approximately 400 variants have been found.[2,3] G6PD deficiency in the newborn

was first descried by Doxiades in 1961. G6PD enzyme plays an important role in the pentose phosphate pathway of glucose metabolism and its deficiency results in the instability of reduced glutathione in red blood cells leading to haemolysis. G6PD deficiency is one of the important causes of neonatal hyperbilirubinaemia. Because of hemolytic nature of the jaundice the hyperbilirubinaemia is only indirect and the serum bilirubin level is often high, requiring phototherapy and sometimes exchange blood transfusion.[4]

It is seen particularly in Mediterranean and oriental ethnic group. Jaundice usually appears within 1st 48 hours of life. Often no exposure to oxidant drugs is identified. However in some cases it is precipitated by administration of vitamin K analogues and the use of antiseptic umbilical paints containing in aniline dyes. G6PD deficiency is more common among the jaundiced babies than in the non-icteric newborns.[5] In Pakistani newborn babies it is also one of the common etiologic factor for neonatal hyperbilirubinaemia.[6] A number of other studies conducted around the world revealed that G6PD deficiency is an important cause of neonatal hyperbilirubinaemia.[7-18] However there is very limited data on the incident of G6PD deficiency in Pakistani icteric newborn. Therefore a study of erythrocyte G6PD deficiency was set up in the icteric newborn babies admitted to the neonatal unit of Khyber Teaching hospital with particular emphasis on its role in the etiology of neonatal hyperbilirubinaemia.

MATERIAL AND METHODS

This study was conducted in the neonatal unit of Khyber Teaching Hospital from July 1998 to June 1999. During this period about 200 neonates with jaundice were studies. The population group comprised of full term neonates born in the same hospital as well as those brought from different other parts of the NWFP. Both Pakistanis and Afghan babies were included in it.

On admission to the hospital detail information regarding gestational age, sex, address, place of birth (home or hospital), age of onset of jaundice, other associated symptoms, feeding, drugs administered etc was elicited. These babies were then subjected to the relevant investigations like complete blood count, serum bilirubin level both direct and indirect, baby and mother blood groups and G6PD enzyme estimation. G6PD enzyme was estimated in the same laboratory using "sigma Diagnostic G6PD reagent for the qualitative, visual, calorimetric determination of G6PD deficiency in red cells"

Interpretation of test result:

Decolourization time

20-60min——— Normal

>60 min————Deficient

Inclusion Criteria: All those neonates with signification indirect hyperbilirubinaemia needing phototherpay were included. These were all full term babies.

Exclusion Criteria: Premature jaundiced babies, those with neonatal sepsis, meningitis or congenital anomalies were excluded from the study. Decision regarding treatment (Phototherapy and/or exchange blood transfusion) were made on the bias of age the babies and serum indirect bilirubin levels.

RESULTS

Total bout 200 babies with neonatal hyperbilirubinaemia were studied. Their age at admission to the hospital ranged from 1-7 days (mean 4.7 days). The

Total No. of Patients	200
No. of babies deficient in G6PD	26
Percent deficient	13%

TABLE – 1

commonest age was 4-7 days (19 babies; 73%) followed by 1-3 days (27%). Out of these 200 jaundiced babies 26(13%) were found to be deficient in G6Pd enzyme.

Among the deficient babies 23(88.5%) were male while 3(11.5%) were female. Twenty (77%) were Pakistani while 6(23%) were Afghan babies. Sixteen (62%) were delivered at home while 10(38%) were hospital born. Twenty four (92%) were through normal vaginal delivery while cesarean section was performed in the rest of the two. Twenty babies (77%) were exclusively breast fed while other foods like green tea, ghutti, bartang etc were given along with breast milk in the remaining six babies (23%). No significant history of drug ingestion could be elicited in their mothers. Injection vitamin K was administered in 4 babies (15%). In none of these babies blood group incompatibility was present between them in their mothers.

Age of appearance of jaundice varied from within 1st 24 hour of life up to 5 days (mean 2 ½ days). In 6 babies (24%(jaundice was noticed within 1st 24 hours. In 7 babies (27%) on the 2nd day of life; in 6(23%) on 3rd day; in 5(20) on the 4th day and in 2(7%) on the 5th day of life.

Men haemoglobin level was 12 gm%. Serum indirect bilirubin level ranged from

SEX DISTRIBUTION OF G6PD DEFICIENT BABIES

Sex	No.	%
Male	23	88.5
Female	3	11.5
Total	26	100

TABLE – 2

AGE OF APPEARANCE OF JAUNDICE

Age (days)	No. of Patients	%
Within 1st 24 hours	6	23
2nd	7	27
3rd	6	23
4th	5	20
5th	2	7

TABLE – 3

7.4mg% to 39mg% (mean 18.7%). Seventeen (65%) babies developed severe hyperbilirubinaemia (serum bilirubin level more than 20mg%) and were given exchange blood transfusion.

61-90min in 17 babies (65%)

90-120min in 3 babies (12%)

>120min in 6 babies (23%)

All of them received phototherapy. Duration of phototherapy ranged form 2-7 days (mean 4 days). Total about 22 exchange blood transfusions were performed din 17 babies. Four babies required more than one exchanges.

Two babies (8%) developed kernicterus. Average hospital stay was 5 days (range 3-7 days).

DISCUSSION

According to this study the incidence of G6PD deficiency in icteric newborn infants is 13%. This figure is slightly higher than the previous studies done in Peshawar by Imran et al. 1984[6], who has reported its

SERUM INDIRECT BILIRUBIN LEVEL (SBL)

Grade	SBL (mg%)	No. of Patients	%
Mild to moderate	<20	9	35
Severe	>20	17	65

TABLE – 4

RED CELL G6PD ACTIVITY

Decolorization time (min)	No of Patients	%
60–90	17	65
90–120	3	12
>120	6	23

TABLE – 5

incidence in the jaundiced neonates as 12%. Another study done by Parveen A et al. 1986[19] shows an incidence of 12.1%. These variations may be due to difference in the genetic make-up of societies, socio-cultural differences, frequency of carrier individuals, sample size, method used for G6PD enzyme estimation and detection rate. This high incidence of G6PD deficiency among the jaundiced babies also shows that neonatal jaundice is the commonest presentation in our set up.

Age at presentation or admission to the hospital raged from 1 to 7 days while the commonest age of appearance of jaundice was the 2nd day of life and by the 5th day of life jaundice has appeared in all these babies. This is the observation of other workers as well (Imran et al 1984 and Parveen et al (1986) and this shows that jaundice appears early in G6PD deficiency.

Twenty three of the deficient babies were male while only 3 were female with overall male to female ratio of 7:6:1. Imran et al 1984 has also reported almost the same ratio i.e 7:1. This observation further supports the x-lined recessive mode of inheritance of this enzymopathy.

Seven (23%) were Afghan babies coming from Peshawar and nearby areas.

TREATMENT GIVEN TO THE G6PD DEFICIENT JAUNDICED BABIES

Treatment modality	No of Patients	%
Phototherapy	26	100
Exchange blood transfusion		

TABLE – 5

This figure is quite significant and it shows that G6PD deficiency is quite common in people belonging to Afghan nationalities, although the exact data in literature in not available so far. No significant history of drug ingestion was elicited in the mothers of these neonates. Also in the babies themselves, injection vitamin k was administered only in four babies (15%). This finding supports the experience and observation of other workers that the haemolyis in G6PD deficient newborns is spontaneous without significant drug history. Most of the babies were exclusively breast feed. We feel transfer of drug in the mother milk may occur. However in 23% of the babies additional foods were also given. Thus there is a need for proper health education and discouragement of traditional first feed. In none of these babies blood groups incompatibility was present between the babies and their mothers, excluding isoimmune haemolysis as a cause of neonatal jaundice. Majority of these babies presented to the hospital with only jaundice as the sole complaint. Mean hemoglobin level was at the lower of the normal limit for age and sex. This might be due to haemolysis.

G6PD enzyme activity ranged from more than 60 minutes to more than 2 hours. This has been the observation in the other studies done in the past (Imran et al 1984 and Parveen a et al 1986).

Hyperbilirubinaemia in G6PD deficiency is indirect and it is quite often severe. In my study serum indirect bilirubin was significantly high and 65% of the babies developed severe hyperbilirubinaemia necessitating exchange transfusions.

Phototherapy was given to all the babies and it was found quite effective in reducing the serum indirect bilirubin level. Mean duration of phototherapy was 4 days and no untoward effect was noted with its use.

When serum bilirubin level reaches> 20mg%, exchange blood transfusion is considered. In this study about 17 babies (65%) developed severe hyperbilirubinaemia and total about 22 exchange blood transfusions were performed. In minority of babies hyperbilirubinaemia persisted after the first exchange transfusion and were given another transfusion (3 babies), while one baby needed total of three transfusions. This procedure was found highly effective in reversing the serum indirect hyperbilirubinaemia. The incidence of reported complications with exchange blood transfusion were negligible. Two babies (8%) developed kernicterus. Both were having severe hyperbilirubinaemia and seeking medical advice and hospital admission was delayed. They were having the early signs of bilirubin encephalopathy. Even then exchange blood transfusion was tried in the hope of reversing their hyperbilirubinaemia.

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