FREQUENCY OF GLUCOSE 6 PHOSPHATE DEHYDROGENASE DEFICIENCY IN NEONATAL JAUNDICE

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ABSTRACT

Objective: To determine the frequency of Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency in neonates presenting with jaundice.

Material and Methods: This descriptive study was conducted at Special Care Baby Unit (SCBU) Department of Child Health, Khyber Teaching Hospital, Peshawar from January 2008 to June 2008. A total number of 283 newborns, aged 1-14 days of either sex admitted with jaundice were included in the study. Biodata and clinical profile of all patients were collected on preformed proforma. G6PD decolorization time, baby and mother blood group, haemoglobin, total bilirubin, retic count and other related investigations were done.

Results: During the study time a total number of 710 newborns was admitted to Special Care Baby Unit. Out of the total special care baby unit admissions, 283(39.85%) neonates had jaundice. Among these 283 jaundiced newborn babies, 83 were G6PD deficient, male were 63 (75.9%) and female were 20 (24.1 %). All jaundiced neonates received phototherapy. Among G6PD deficient jaundiced babies 54(65.06%) neonates had severe hyperbilirubinemia and needed exchange transfusion. Nine babies (10.84%) developed kernicterus. G6PD discoloration time test at the time of admission varied from 60-120 minutes. Serum bilirubin level ranged from 9.5-40 mg/dl.

Conclusion: G6PD deficiency is a relatively common cause of neonatal jaundice and is more frequent in male babies. Neonates suffering from G6PD deficiency present with early jaundice like other hemolytic causes of jaundice including ABO and Rh incompatibility.

Key Words: Neonatal Jaundice, Glucose 6 Phosphate Dehydrogenase, Hyperbilirubinemia. Phototherapy.

INTRODUCTION

Glucose 6 Phosphate dehydrogenase deficiency was first discovered in 1950, but the history goes back 2000 years when Egyptian priests were not allowed to take broad beans because of occurrence of disorder now called as acute hemolytic crisis\(^1\). G6PD is a cytosolic enzyme encoded by X-linked gene and expressed in all tissues of the body\(^2\). G6PD deficiency is the commonest enzyme defect\(^3,4\) not only in hematology but also in human physiology as a whole\(^5\). G6PD catalyzes the first step in pentose phosphate pathway, generating nicotinamide adenine dinucleotide phosphate (NADPH), which keeps the glutathione in reduced form which has got protective role for red blood cells and other tissues from oxidative damage caused by medicines, infections and environmental stresses\(^6\).

The normal enzyme type found in Caucasians is G6PD-B\(^-\). G6PD gene is extremely polymorphic with over 130 mutations\(^8\) and approximately 400 variants. In majority of cases these variants are due to structural gene mutation caused by single amino acid substitution\(^9\). G6PD deficiency is most common disorder and 400 million people throughout the world are affected in different parts of the world\(^10\). The prevalence rate varies from as high as 62 % among Kurdish Jews to as low as 0.1% in Japan, while it ranges from 3 to 6.9% in Pakistan, Southern China and Southern Russia\(^11\). The commonest presentation of G6PD deficiency in Pakistan is neonatal jaundice and acute hemolysis\(^12\).

Neonatal Jaundice is an important condition and accounts for a large number of special care baby unit admissions. Neonatal jaundice commonly presents in the first week of life. Pathological jaundice even appears on the first day of life and can lead to complications if no proper intervention is taken timely. Serum hyperbilirubinemia is defined as total serum bilirubin (TSB) level above 95 centile for that specific age in hours, occurring in 8-9 percent of neonates during the first week of life\(^13,14\). If the jaundice progresses and the serum bilirubin level exceed 25-30 milligram / deciliter (mg/dl) i.e. greater than 99\(^{th}\) centile, even healthy neonates are prone to develop neuronal damage leading to kernicterus, unless proper...
interventional measures are taken\textsuperscript{14}. Indirect bilirubin content of the total serum bilirubin level is notorious component because it crosses blood brain barrier and accumulates in the nervous tissue, causing irreversible damage to neuronal tissue and resulting in kernicterus. Several factors are responsible in neonates to develop hyperbilirubinemia including imbalance between production, conjugation and elimination of bilirubin, environmental factors and ethnicity\textsuperscript{15}. G6PD deficiency is one of the common aetiologic factors for neonatal hyperbilirubinemia in our country, however the data is limited. This study was conducted to determine the relative frequency of G6PD deficiency in neonatal jaundice.

**MATERIAL AND METHODS**

This hospital based descriptive study was conducted at Special Care Baby Unit, Department of Child Health Khyber Teaching Hospital, Peshawar, from January 2008 to June 2008. All full term neonates age 1-14 days who presented with jaundice were included in the study. Low birth weight babies, neonates with congenital anomalies such as cleft palate, neonates with Down’s syndrome, biliary atresia, hypothyroidism and neonatal hepatitis syndrome were excluded from the study. Complete history, detailed examination and investigations of every neonate were recorded on proforma including sex, age, appearance of jaundice, time of admission and any history of jaundice and exchange transfusion in other siblings. The investigations done in these jaundiced babies were blood groups of the baby and mother, G6PD, full blood count (FBC), retic count and serum bilirubin total and direct, indirect.

G6PD enzyme estimation was done in minutes using Sigma Diagnostic G6PD reagent. The test vial were observed at 25 minutes intervals up to one hour for a change of color from its original deep blue to a maroon or reddish end point. The individual reactions were classified as normal or G6PD deficient based on their dye-decolorization time. Change of color within one hour indicated normal level of glucose-6-phosphate dehydrogenase. The samples that did not decolorize after 70 minutes were labeled as G6PD deficient.

**RESULTS**

The total number of babies admitted to special care baby unit during the study period was 710. Out of these 283(39.85%) neonates were admitted with jaundice. Causes of neonatal jaundice are shown in Table 1. Amongst the G6PD deficient male neonates were 63 (75.9%) and the female were 20 (24.1%). Hemoglobin, retic counts, total bilirubin and G6PD of the jaundiced neonates is given with mean, standard deviation and range in Table 2. The mean age of appearance of jaundice in G6PD deficient babies was 1.85 ± 0.74 days while the range was 1-3.5 days. The mean age of the jaundiced neonates at the time of admission was 6.29 ± 2.69 days while the range was 1-14 days. All the babies received photo therapy. Among 83 G6PD deficient neonates 54 (65.06%) babies with severe hyperbilirubinemia required exchange blood transfusions. Exchange blood transfusion was done once in 49 patients (59.04%) while in rest five cases (6.02%) it was done more than once, as shown in Figure 1. Nine G6PD deficient neonates (10.84%) developed Kernicterus.

**DISCUSSION**

In this study neonatal jaundice constituted 40% of special care baby unit admissions which is a

**Table 1: Causes of Neonatal Jaundice n=283**

<table>
<thead>
<tr>
<th>Causes of Jaundice</th>
<th>No. of patients and percentage</th>
</tr>
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<tbody>
<tr>
<td>G6PD deficiency</td>
<td>83 (29.3%)</td>
</tr>
<tr>
<td>ABO Incompatibility</td>
<td>72 (25.4%)</td>
</tr>
<tr>
<td>Rh Incompatibility</td>
<td>35 (12.4%)</td>
</tr>
<tr>
<td>Other Causes</td>
<td>93 (32.9%)</td>
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<tr>
<td>Total</td>
<td>283 (100%)</td>
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</tbody>
</table>

**Table 2: Laboratory Profile with Mean and Range in G6PD Deficient Jaundiced Neonates**

<table>
<thead>
<tr>
<th>Test (Unit)</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (gm/dl)</td>
<td>16.53 ± 4.25</td>
<td>12-18.5</td>
</tr>
<tr>
<td>Reticulocyte Count</td>
<td>4.50 ± 1.25</td>
<td>2-8.5</td>
</tr>
<tr>
<td>Serum Total Bilirubin (mg/dl)</td>
<td>19.5 ± 6.54</td>
<td>7.5-30.5</td>
</tr>
<tr>
<td>G6PD Discoloration Time (in Minutes)</td>
<td>92.92 ± 23.07</td>
<td>60-120</td>
</tr>
</tbody>
</table>

**Fig. 1: Therapeutic Modalities in Jaundiced Neonates with G6PD deficiency n = 83**
significant number. A study conducted at Nursery Unit Lady Reading Hospital by Hussain M et al showed that neonatal jaundice constituted 23% of the nursery admission. Several other international studies support our study regarding neonatal jaundice as an important cause of special care baby unit admission. Neonatal jaundice has got several causes. In our study we found three important causes of early neonatal jaundice i.e. G6PD deficiency, ABO and Rhesus incompatibility. Almost same etiologies of neonatal jaundice have been mentioned in various national and international studies.

Frequency of G6PD deficiency was an important variable of our study. In our study we found that G6PD deficiency made a big proportion of the jaundiced neonates i.e. 29.3%. The data regarding frequency of G6PD deficiency is different from various parts of our country and abroad. The frequency was 12%, 13%, 14% and 16% in national studies conducted by Imran et al, Khan A et al, Rehman G et al and Hussain M et al respectively. These figures are comparatively lower than our ones. Various reasons may be responsible for increasing frequency. Studies data available on various ethnic groups show high frequency in Pathans as compared to rest of the ethnic groups of the country and secondly the figures are rising because of interfamily marriages, in our part of the country. International data regarding the G6PD deficiency frequency varies a lot. Studies from Saudi Arabia, Iran, India show frequency of G6PD deficiency as low as 2%, 2.1% and 7.5% respectively. On the other hand studies in China, Nigeria and Thailand found high occurrence of G6PD deficiency with figures of 18.42%, 25.5% and 38% respectively.

Gender wise distribution varies in G6PD deficiency. As it is a sex linked recessive disorder so it is obvious to be pathology of the male sex. But females are not excluded. In our study male to female ratio was almost 3:1. The sex ratio has varied in different studies. A study conducted at District Timergara by Rahim F et al shows ratio of 7:1. The same results have been given by Ahmed I et al. The difference between ratios of male to female is quite high to our ones. However, another study shows the difference much lower with male to female ratio of 2:1.

Neonatal jaundice appeared early in our study. Almost same was finding in other hospital based studies, while in another study presentation was almost same. In our study we found three important causes of early neonatal jaundice and ultimately reversing bilirubin encephalopathy (kernicterus). Kernicterus due to G6PD deficiency has also been reported by Khan A in 2002. In rest of the studies photo therapy and exchange transfusion were very effective in reducing the serum bilirubin and preventing kernicterus in all babies with severe hyperbilirubinemia.

CONCLUSION

Early recognition of the G6PD deficiency and management will significantly reduce the morbidity and mortality related to severe hyperbilirubinemia due to G6PD deficiency.

REFERENCES


