GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY IN NEONATES PRESENTING WITH JAUNDICE

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ABSTRACT

Objective: To determine the frequency of Glucose-6-phosphate dehydrogenase (G6PD) deficiency in infants presenting with jaundice.

Material and Methods: This retrospective study was conducted in Fazal Rahim Clinical Laboratory Timergara District Dir North West Frontier Province of Pakistan, from 1st January 2004 to 31st December 2004 on 120 neonates. Data regarding sex and age, serum bilirubin total, serum bilirubin direct and G6PD status was extracted using database software designed by the principal author. The inclusion criterion was neonates with high serum bilirubin and G6PD test performed simultaneously. The exclusion criterion was premature babies and incomplete request forms. Microsoft Excel 2000 was used for data analysis

Results: Out of 120 patients, 97 (80.8%) were male and 23 (19.2%) were female ranging in age from 3 – 10 days with mean 6.5 days and median 5 days.

Thirty two (26.6%) neonates were found G6PD deficient. Among patients with normal G6PD level male to female ratio was 3.63:1. In G6PD deficient patients male to female ratio was 7:1. The serum bilirubin of the G6PD normal patients was 12.8 + 5.0 mg/dl and that of G6PD deficient patients was 13.5 + 6.8 mg/dl.

Conclusion: G6PD deficiency is quite high in neonates presenting with jaundice. The diagnosis is simple and if left undetected may cause serious consequences in situations of oxidant stress.

Key Words: Neonates, Jaundice, G6PD deficiency.

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) is the first enzyme in the hexose monophosphate shunt of the Embden-Meyerhof pathway from which red cells derive most of their metabolic energy. The function of this shunt is to provide NADPH for reduction of oxidized glutathione through glutathione reductase thus protecting the red cells against oxidative damage[1]. This protective mechanism is crippled in the absence of G6PD and certain drugs in sufficient concentration can seriously injure the erythrocytes resulting in haemolysis and jaundice[2]. The deficiency is inherited as an X-linked disorder. A total of 400 million persons are affected by this disorder worldwide[3]. In the United States of America 2.5% of males and 1.6% of females are deficient, with most having only moderate enzyme deficiency. African American males (12.2%) and females (4.1%), along with Asian males (4.3%), have been reported to have the highest rates of G6PD deficiency[4]. In some parts of China the mutation frequency of male G6PD-deficient individuals was observed to be 7.43%[5].

In Pakistan the prevalence of G6PD deficiency is reported by several authors as Khan and Khawar (2002) 13%[6], Imran et al (1984) 12%[7], Parveen et al (1986) 12.1%[8], Khattak et al. (2006)12%[9], Alvi et al. (2006) 10% [10], and Rashid et al. (2005) as 06%[11].

Infants with G6PD deficiency may have significant hyperbilirubinuria and may require phototherapy or exchange transfusion to prevent kernicterus. Hemolysis is not the main determinant of neonatal jaundice in G6PD-deficient babies[12]

Infants with the severe variant of glucose-

FREQUENCY OF G6PD DEFICINECY

Group	Number	%age	Male	Female	M:F ratio
Total Patients	120	100	97	23	4.2 :1
G6PD Normal	88	73.3	69	19	3.6:1
G6PD Deficient	32	26.7	28	04	7:1

Table 1

6-phosphate dehydrogenase (G6PD) deficiency may develop hyperbilirubinaemia sufficiently severe to cause kernicterus and death, acute haemolysis on exposure to oxidant stress, congenital non-spherocytic haemolytic anaemia and, rarely, increased susceptibility to bacterial infection. In spite of these potential problems, G6PD deficiency is often not included among screening programmes for inherited disorders[13].

G6PD deficient newborns are more prone to develop neonatal jaundice which is, on its own, no more severe than jaundice from other causes.[14,15], In cases of oxidant stress due to various drugs, bees stings or Fava beans the patient may develop life threatening acute haemolytic crises.[16]

It was observed by some of the authors that the frequency of G6PD deficiency is more in icteric patients that in nonicterics. Therefore the preexisting available data at Fazal Rahim Clinical Laboratory, which is a referral laboratory in the area, was evaluated for G6PD deficiency in infants presenting with jaundice.

MATERIAL AND METHODS

This is a computer based retrospective study at Fazal Rahim Clinical Laboratory which is a reference clinical laboratory in Timergara District Dir (lower) NWFP, from January 1st 2004 till December 31, 2004. The patients were those who were referred for investigations and having the relevant data in the request form.

A Computer database program designed by the principal author was used to extract the data. The data extracted included sex, age, serum bilirubin total, serum bilirubin direct and G6PD status.

All those patients were included in the study who had jaundice and G6PD test had been done. All those babies were excluded from the study who were premature, or those babies whose relevant data was not available in the request form.

Microsoft Excel 2000 was used for data analysis

RESULTS

The total number of patients who were jaundiced and having G6PD test performed were 120. There were 97 (80.8%) male and 23 (19.2%) female with a male to female ration of 4.2:1. Age ranged from 3 – 10 days with mean age of 6.5 days and median 5 days. Thirty two (26.6%) were G6PD deficient. Among patients with normal G6PD level male to female ratio was 3.63:1. In G6PD deficient patients male to female ratio was 7:1, which is significant (table No.1). The total serum bilirubin of the total jaundiced patients was 13.0 $\pm$ 5.6 mg/dl, of the G6PD normal patients 12.8 $\pm$ 5.0 mg/dl and that of G6PD deficient patients was 13.5 $\pm$ 6.8 mg/dl (table No.2). Eleven patients (34.4%) had serum bilirubin $\leq$10 mg/dl, 18 (56.25%) 10.1 to 20 mg/dl, 2 (6.25%) 20.1 to 30 mg/dl and only one case has serum bilirubin above 30 mg/dl (table No.3).

Comparing the values of total serum bilirubin the difference was not significant amongst the various groups (tables No 4).

DISCUSSION

In this study the prevalence of G6PD deficiency in neonates with jaundice was found in 26.6% of patients. Khan A et al[6] in 2002 reported G6PD deficiency in 13% at Peshawar. Imran et al[7] reported as 12%, and Parveen et al as 12.1%[8],

SERUM BILIRUBIN TOTAL

Range mg /dl	No	%age	Cumulative No.	Cumulative %age
Upto 10.0	11	34.37	11	34.37
10.1 - 20.0	18	56.25	29	90.62
20.1 - 30.0	02	6.25	31	96.87
30.1 - 40.0	01	3.12	32	100

Table 2

STATISTICAL VALUES SERUM BILIRUBIN TOTAL (mg/dl)

Parameter	Range	Mean	Standard deviation
Total Patients	4.2 - 38	13.08	5.6
G6PD Normal	4.2 - 25.6	12.86	5.0
G6PD Deficient	4.9 - 38	13.5	6.8

Table 3

STATISTICAL VALUES: COMPARISON OF TWO MEANS (P VALUE) SERUM BILIRUBIN TOTAL mg/dl

	Pair	P value
1	G6PD Deficient and Total	>0.05 (N.S)
11	G6PD Normal and Total	>0.05 (N.S)
111	G6PD Deficient and G6PD Normal	>0.05 (N.S)

N.S = statistically not significant

Table 4

Alvi et al[10] in 2006 observed 10% at Lahore and Rashid et al[11] 2005 as 06%. Khattak et al[9]. Observed G6PD deficiency in 12% patients with haemolytic anaemias.

Our data of 26%, is quite higher than, reported by others [6-10]. The reasons may be that the 1st cousin marriage is common in this society. The other reason is that the study conducted by Khatak et al[9] was on general population. The frequency of G6PD deficiency in Pathans in this study was reported as 8.3%. The frequency of G6PD deficiency is higher in patients with jaundice than in general population. If the prevalence of 8.3% in Pathans, is considered to be accurate and also higher incidence of jaundice in G6PD deficient patients, then the frequency of 26% can be explained.

G6PD deficiency in patients with neonatal jaundice varies amongst many countries ranging from10.6% in UAE (Dawodu et al 1998)[16] ,Taiwan Male 11.3% female 7%[12], Jamacia 22% (Gibbs et al 1979)[17], Papua New Guinea 22%[18], Basrah 51%[19] and Nigeria 62%[20].

Khan TA et al[21] reported the frequency of G6PD deficiency in anaemic patients at Batkhela Malakand Agency as 3.4% and the overall frequency as 1.36%. According to Ali et al[22] the frequency of G6PD deficiency as 1.8% in general population. Similarly the deficiency state was 1.07% in Kashmiris, 1.47% in Punjabis, 2.77% in Sindhis, and 3.17% in Pathans. Yet in another study by Khan TA et al[21], 5.9% were G6PD deficient. The frequency distribution in Pathans was (8.3%) and in Punjabis (3.5%). (Inter-racial differences in the frequency of G6PD deficiency among the sub groups of Punjabis and Pathans were also noted.)

Over all incidence of G6PD deficiency in India is 1.5%, Pakistan 2%[22], Malays 3.5%, China 4.5%[23], Thailand 3-18 % depending upon geographic distribution (Tanphaichitr 1999) and Saudia 18% (Abu-Osba 1989)[24].

As compared to international data our values of 26.6% comes out to be intermediate. As this is a limited study of only 120 patients, other studies based on large number of patients are suggested to obtain more precise percentage of G6PD deficiency. In this study age ranged from 3 – 10 days with mean 6.5 days and median 5 days. According to Khan A[6] one case of G-6PD deficiency developed jaundice during first 24 hours of life, 8 cases between 1 -7 days and one case after 7 days of life[10]. Age of appearance of jaundice varied from 1st 24 hours of life up to 5 days (mean 2.5 days)[6]. Among patients with normal G6PD level male to female ratio was 3.63:1. In G6PD deficient patients male to female ratio was 7:1. According to Khatak et al. (2006) the male to female ratio was 7:1[9] and according to another study 2:1, at Peshawar the male to female ratio was 7.6:1.[6] Taiwan 2:1[25]

In this study the total serum bilirubin of the total jaundiced patients was 13.0 ± 5.6 mg/dl, of the G6PD normal patients 12.8 ± 5.0 and that of G6PD deficient patients was 13.5 ± 6.8 mg/dl. Comparing the values of total serum bilirubin the difference was not significant amongst the various groups. According to Alvi et al (2006) peak serum bilirubin levels in neonates with G-6PD deficiency were < 20 mg/dl in 2% cases, 20-30 mg/dl in 6% cases and >30 mg/dl in 2% cases[10]. While in another study mean serum bilirubin level was 18.7mg%[6].

CONCLUSION

As obvious from this study as well as other studies quoted, G6PD deficiency is quite high in neonates presenting with jaundice.

REFERENCES

1. Ho HY, Cheng ML, Cheng PF, Chiu DT. Low

oxygen tension alleviates oxidative damage and delays cellular senescence in G6PD-deficient cells. Free Radic Res 2007 ;41:571-9.

2. Ho HY, Cheng ML, Chiu DT. Glucose-6-phosphate dehydrogenase--from oxidative stress to cellular functions and degenerative diseases. Redox Rep 2007;12:109-18.
3. Theodorsson E, Birgens H, Hagve TA. Haemoglobinopathies and glucose-6-phosphate dehydrogenase deficiency in a Scandinavian perspective. Scand J Clin Lab Invest 2007;67 :3-10.
4. Chinevere TD, Murray CK, Grant E, Johnson GA, Duelm F, Hospenthal DR. Prevalence of glucose-6-phosphate dehydrogenase deficiency in U.S. Army personnel. Mil Med 2006 ;171:905–7.
5. Yan T, Cai R, Mo O, Zhu D, Ouyang H, Huang L et al. Incidence and complete molecular characterization of glucose-6-phosphate dehydrogenase deficiency in the Guangxi Zhuang autonomous region of southern China: description of four novel mutations. Haematologica 2006;91:1321 - 8.
6. Khan A, Khawar N. Neonatal Hyperbilirubinaemia secondary to Erythrocyte Glucose-6-Phosphate Dehydrogenease deficiency. J Postgrad Med Inst 2002;16:33-8.
7. Imran M, Rashid, Akbar A. Neonatal jaundice due to G6PD deficiency. Pak Paed J 1984;8:126-8.
8. Parveen A, Azra A, Ahmad KN.G6PD status and neonatal hyperbilirubinaemia. Pak Paed J 1986;10:241-4.
9. Khattak MI, Ishaq T, Subhan M, Afridi J. The frequency and age presentation of G6PD deficiency in 200 patients of hemolytic anemia. J Postgrad Med Inst 2006;20:170-3.
10. Alvi MY, Laeeq A, Khan MA, Iqbal MA. Glucose 6 – Phosphate dehydrogenase deficiency associated with neonatal jaundice Pak Paed J 2006;30:28-33.
11. Rasheed S, Hayee A, Lodhi Y, Ahmed R. Neonatal jaundice and glucose-6-phosphate dehydrogenase deficiency. Ann King Edward Med Coll 2005;11:566-7.
12. Jalloh S, Van Rostenberghe H, Yusoff NM, Ghazali S, Nik Ismail NZ, Matsuo M, Wahab NA, Nishio H. Poor correlation between hemolysis and jaundice in glucose 6-phosphate dehydrogenase-deficient babies. Pediatr Int 2005;47:258 - 61.
13. Mallouh AA, Imseeh G, Abu-Osba YK, Hamdan JA. Screening for glucose-6-phosphate dehydrogenase deficiency can prevent severe neonatal jaundice. Ann Trop Paediatr 1992;12:391 - 405.
14. Kaplan M, Beutler E, Vreman HJ, Hammerman C, Levy-Lahad E, Renbaum P, Stevenson DK. Neonatal hyperbilirubinemia in glucose-6-phosphate dehydrogenase-deficient heterozygotes. Pediatrics. 1999 ;104:68-74.
15. Tanphaichitr VS. Glucose-6-phosphate dehydrogenase deficiency in Thailand; its significance in the newborn. Southeast Asian J Trop Med Public Health. 1999;30 Suppl 2:75-8.
16. Dawodu A, Qureshi MM, Moustafa IA, Bayoumi RA. Epidemiology of clinical hyperbilirubinaemia in Al Ain, United Arab Emirates. Ann Trop Paediatr 1998 ;18:93 - 9.
17. Gibbs WN, Gray R, Lowry M. Glucose-6-phosphate dehydrogenase deficiency and neonatal jaundice in Jamaica. Br J Haematol 1979 ;43:263-74.
18. Woodfield DG, Biddulph J. Neonatal jaundice and glucose-6-phosphate dehydrogenase deficiency in Papua New Guinea. Med J Aust 1975;1:443-6.
19. Al-Naama LM, Al-Sadoon IA, Al-Naama MM. Neonatal jaundice and glucose-6-phosphate dehydrogenase deficiency in Basrah. Ann Trop Paediatr 1987 ;7:134 - 8.
20. Dawodu AH, Owa JA, Familusi JB. A prospective study of the role of bacterial infection and G6PD deficiency in severe neonatal jaundice in Nigeria. Trop Geogr Med 1984 ;36:127-32.
21. Khan TA, Ahmed S, Anwar M, Ayub M. The frequency of Glucose-6 Phosphate Dehydrogenase deficiency in Punjabis and Pathans. J Postgrad Med Inst 2004;18:592-7.
22. Ali N, Anwar M, Ayyub M, Bhatti FA, Nadeem M, Nadeem A. Frequency of Glucose-6-Phosphate Dehydrogenase deficiency in some ethnic groups of Pakistan. J Coll Physicians Surg Pak 2005;15:137-41.
23. Niazi GA, Adeyokunnu A, Westwood B, Beutler E. Neonatal jaundice in Saudi newborns with G6PD Aures. Ann Trop Paediatr 1996 ;16:33 - 7.
24. Hon AT, Balakrishnan S, Ahmad Z. Hyperbilirubinaemia and erythrocytic glucose 6 phosphate dehydrogenase deficiency in Malaysian children. Med J Malaysia 1989; 44:30 - 4.

25. Abu-Osba YK, Mallouh AA, Hann RW. Incidence and causes of sepsis in glucose-6-phosphate dehydrogenase-deficient newborn infants. J Pediatr 1989 ;114:748 - 52.

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