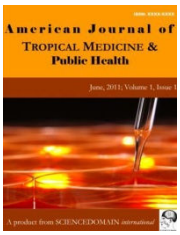

American Journal of TROPICAL MEDICINE & Public Health
1(3): 73-78, 2011

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Evaluation of Glucose- 6- Phosphate Dehydrogenase Deficiency in Icteric Newborns in Nigeria

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Research Article

Received 19th June 2011
Accepted 19th July 2011
Online Ready 9th August 2011

ABSTRACT

Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is one of the most important causes of neonatal jaundice in Far Eastern, Mediterranean and African countries including Nigeria. Although neonatal jaundice is common in our area of practice (Rivers state), no documentation has been made of the prevalence of G6PD deficiency and its contribution to neonatal jaundice in Port Harcourt, Nigeria.
Aims: The aim of this study was to determine the prevalence G6PD deficiency among neonates at University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Nigeria.
Study design: Descriptive cross-sectional study.
Place and Duration of Study: Special Care Baby Unit of UPTH, Port Harcourt, Nigeria between January 2006 to December 2006.
Materials and Methods: We included 400 neonates with jaundice. Jaundice was assessed clinically and confirmed by laboratory estimation of serum bilirubin. G6PD enzyme activity was assayed quantitatively using the method of Kombery.
Results: A total of 400 neonates comprising 288 (78.0%) males and 112 (28.0%) females were recruited into the study. The male/female ratio was 2.6:1. Of these, two hundred and eight (52.0%) were born in UPTH, the study site while 192 (48.0%) were born in other hospitals but referred and admitted into SCBU of UPTH. A total of 210 neonates were G6PD deficient giving a prevalence of 52.5%. Among the G6PD deficient neonates, 145 (69.0%) were males while 65(31.0%) were females. The mean level of G6PD activity for the deficient neonates was 17.3 ± 10.9 %. Levels of enzyme activity were significantly lower in affected males than in the affected females ($P<0.05$).
Conclusion: There is a high prevalence of G6PD deficiency among neonates seen at the

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UPTH, in Port Harcourt, Nigeria. This calls for routine screening of every new born for the enzyme deficiency.

Keywords: Glucose 6-phosphate dehydrogenase deficiency; jaundice; neonates;

1. INTRODUCTION

Glucose 6-phosphate dehydrogenase is an enzyme found in normal red blood cells. Its primary metabolic role in normal concentration is to protect red cells against oxidative damage. Levels are higher in younger cells than in aging red cells. In some individuals, the level of the enzyme activity is low due to a deficiency of the enzyme. In such persons, the protective effect of the enzyme on the red cell is lost and it becomes susceptible to oxidative damage when in contact with oxidative agents. G6PD deficiency is the commonest inherited red cell enzymopathy world wide (Segel, 2004). It affects around 400 million people globally with the highest prevalence in the tropics and subtropics (Ademowo and Falusi, 2002). It is an X-linked disorder, thus manifesting in hemizygous males and homozygous females. However, approximately 10% of heterozygous females may also be at risk. The presentation is variable depending on the residual enzyme activity and ranges from completely asymptomatic individuals to those who have lifelong haemolysis. Most significant manifestations are drug-induced haemolysis, favism, neonatal hyper bilirubinaemia and non spherocytic haemolytic anaemia (Luzzatto and Gordon-Smith, 2001; Kaplan and Hammerman, 2004).

Severe neonatal jaundice (NNJ) remains an important cause of hospitalization in the first week of life particularly in developing countries where glucose-6-phosphate-dehydrogenase (G6PD) deficiency is prevalent (Sarreshtedari and Dolatshahi, 2004). NNJ is seldom associated with mortality when closely monitored but portends significant long-term risks in settings where hospitals are ill-equipped to provide phototherapy or exchange blood transfusion (Badens et al., 2001). Whilst investment in the development of low-cost bilirubin monitoring devices, functional phototherapy units at first-level health facilities and improved care-seeking practices are also essential in the management of neonatal jaundice, particularly in sub-Saharan Africa, early detection of the at-risk populations like the G6PD deficient neonates is an important first step towards redressing the current lack of global initiatives on NNJ.

Early detection of the at-risk populations helps in prevention of morbidity associated with the enzyme deficiency. One way of detecting the at-risk is by screening newborns. Newborn screening for G6PD deficiency has been implemented and incorporated into the screening program in several countries, such as in the Middle East, Eastern Europe and Southeast Asia (Kaplan and Hammerman, 2004). This is however not the situation in Nigeria. The aim of this study was to determine the prevalence of G6PD deficiency and the mean level of enzyme activity in the newborns seen at the University of Port Harcourt Teaching Hospital, Nigeria. Information obtained would be used for advocacy.

2. MATERIALS AND METHODS

This was a prospective study conducted at the Special Care Baby Unit (SCBU) of the University of Port Harcourt Teaching Hospital (U.P.T.H) Nigeria. The Teaching Hospital is the only tertiary hospital located in Port Harcourt, the capital of Rivers State of Nigeria and serves as a referral centre for the neighbouring states of Abia, Bayelsa, Imo, Akwa Ibom and Delta. Approximately 3,500 infants are delivered each year. Ethical approval was obtained from the Ethical Committee of UPTH for this study.

Neonates (within 28 days of life) with clinical and laboratory evidence of jaundice were enrolled into the study and the usual work-up for neonatal jaundice in our hospital which includes a complete blood count, blood groups of mother and infant, Coombs'test, serum bilirubin (total and conjugated) and G6PD assay were carried out.

Data on mother and neonate with regards to sociodemographics, exposure to icterogenic substances, and age at onset of jaundice were collected using a structured questionnaire. Bilirubin was estimated using the Van den Bergh diazo reaction (Afolayan and Luzzatto, 1971). G6PD assay was based on the method of Kornbery et al. (Scriver, 1995). Results were expressed as enzyme units per gram of Haemoglobin (eu/gmhb). Values below 40% of the adult value [8.83± 1.59 eu/gram haemoglobin at 30 ^{0}C (Scriver, 1995)] were regarded as deficient (Fairbanks and Lampe, 1968).

3. RESULTS

Four hundred neonates were recruited into the study from June to December 2006. There were 288 (78.0%) males and 112 (28.0%) females in the study population (Table 1).

Table 1. Characteristics of the Neonates in the study population and their G6PD status

Characteristics	G6PD def neonates	Non G6PD def neonates	p-value
	n = 210	n = 190	
Gender			
Males	145(69.0)	143(75.3)	0.204
Females	65(31.0)	47(24.7)	
Place of Birth			
Inborn	97(46.2)	111(53.3)	0.014
Outborn	113(53.8)	79(41.1)	
Gestational Age in weeks			
< 37 weeks	47(22.4)	29(15.3)	0.070
≥ 37 weeks	163(77.6)	161(84.7)	
Mode of Delivery			
SVD	156 (77.3)	133(70.0)	0.339
CS	54 (22.7)	157(30.0)	
Apgar Scores in minutes			
< 3	26 (12.4)	32 (17.7)	0.316
3 - 6	34(16.2)	30(16.6)	
≥7	150(71.4)	119(65.7)	

Figure in parentheses are percentages of the total.
SVD= Spontaneous vertex delivery; CS = Caesarean section; wks = weeks

Two hundred and eight (52.0%) were inborn while 192 (48.0%) were outborn. Of these, 210 neonates were found to be deficient (145 males and 65 females) while 190 neonates were normal giving a prevalence of 52.5%. The characteristics of neonates (Table1) showed that 97(46.2%) were inborn while 113(52.8%) were out born. Forty one (19.5%) of them were born preterm while 163 (77.6%) were term. Most 156(74.3%) of them were delivered by spontaneous vertex delivery while 54(25.7%) were by caesarian section. Sixty (28.6%) of the G6PD- deficient neonates were asphyxiated ranging from mild to severe.

The mean G6PD level of activity for the deficient neonates was 17.3 ±10.9 %. While the mean for the deficient males and females were 12.4 ±7.7% and 28.5 ±8.5%, respectively. The G6PD enzyme level of activity is shown in table 2.

Table 2. G6PD level of activity in male and female neonates

G6PD level of activity %	Males n = 145 (%)	Females n = 65(%)	Total n = (%)
< 10	61(42.1)	3(4.6)	64(30.5)
10-20	67(46.2)	7(10.8)	74(35.2)
21-30	12(8.3)	22(33.8)	34(16.2)
31 - 40	5(3.4)	35(50.8)	38(18.1)
Total	145(100)	65(100)	210(100)

$\chi^2 = 110.32$; df = 3; p= 0.0000
Figure in parentheses are percentages of the total

4. DISCUSSION

The prevalence of G6PD deficiency varies from one geographical zone to another and between ethnic populations (Cladera et al., 1997). In this study, the overall prevalence of G6PD deficiency was 52.5%. This figure is higher than the prevalence rates reported from Calabar, southern Nigeria (Uko et al., 2004), and 11.5% from the Zambia (Bhagwat and Muleta, 1984). Although Calabar is the same geo-political zone with the present study centre a probable reason for the difference in prevalence rate may be the small sample size of 102 jaundiced neonates in the Calabar study. The Zambian study employed the screening tests method and these are known to have the limitation of missing some heterozygous females and recently transfused children. It is possible that this may have accounted for the lower prevalence in their study compared to ours. Furthermore, the prevalence rate obtained in this study is also higher than those obtained in Spain, France and Thailand which documented prevalence rates of 9.7%, 12.08% and 2.1% respectively. Our study was conducted in Nigeria –a malaria endemic zone while these countries are in the malaria free temperate region thus confirming the association between G6PD deficiency and malaria endemic areas (William, 1983).

The overall prevalence of G6PD deficiency for males was 69% while that of females was 31% in this study. This is consistent with the X- linked recessive inheritance (Maxwell, 1981) of G6PD deficiency which makes it more prevalent in males.

There was a slightly higher frequency of G6PD deficiency among out born babies. This may be explained by the fact that birth circumstances may result in birth asphyxia, acidosis and infection all of which are potential triggers for haemolysis in affected neonates (William, 1983).

The enzyme level of activity was significantly lower in males than females. This is in agreement with a Nigerian study (Egesie et al., 2008) where lower prevalence was reported in males. This is not surprising because one would expect affected males to have lower levels of the enzyme than the females in view of the fact that the defect is X-linked recessive. However, the process of lyonisation is complex and involves random inactivation of an X chromosome. In some instances, more of the maternally derived or paternally derived chromosome may escape inactivation and even a small advantage of one set of clones over the other would result in marked disparity between the number of normal and deficient cells. As a result, affected females can show extremely low levels of the enzyme (Pai, 1980). The mean enzyme activity in the deficient subjects in this study was 17.3 ± 10.9%. This value is comparable with previously documented result which indicated mean values of 5-15% in the A- variant (Pai, 1980).

5. CONCLUSION

This study has shown that a higher proportion of symptomatic (icteric) neonates in our locality have low level of G6PD enzyme activity. Therefore, routine screening for G6PD deficiency in all newborn babies should be mandatory and included in the health care system of Nigeria.

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