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Prevalence of G6PD deficiency in children presenting with jaundice in Ilorin, Nigeria

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ABSTRACT: **Background:** Jaundice is a common presentation in children at the University of Ilorin Teaching Hospital, with a variety of underlying causes including glucose-6-phosphate dehydrogenase (G6PD) deficiency. **Aims of Study:** To determine the prevalence of G6PD deficiency in children presenting with Jaundice in Ilorin, and whether routine screening for G6PD deficiency would be advisable in children presenting with Jaundice. **Patients/Methods:** One hundred children were recruited into the study over a period of one year. The children (male and female) were aged between one day and 15 years; with a mean age of 4.8 ± 5. Screening for G6PD deficiency was carried out using the methaemoglobin reduction method of Brewer. **Results:** The overall prevalence of G6PD deficiency in children presenting with Jaundice was 43.0 percent. Prevalence in males was 50.0 percent and 28.1 percent in females. **Conclusion:** The finding in this study indicates that children in the age group one day to 15 years presenting with jaundice at Ilorin have an overall 43.0 percent [males (50 percent) and females (28.1 percent) chance of having G6PD deficiency, as the underlying cause of their jaundice. This justifies the need for G6PD screening in children presenting with jaundice.

Keywords: Prevalence, G6PD deficiency, Jaundice.

Introduction

Glucose-6-phosphate dehydrogenase (G6PD) is a cytoplasmic enzyme that is essential for red cells capacity to withstand oxidant stress.[1]It represents less than one part in 20,000 of the protein of the cell. The enzyme catalyses the first step in the hexose monophosphate pathway producing reduced nicotinamide adenine dinucleotide phosphate (NADPH); this is responsible for the generation and maintenance of reduced glutathione (GSH). Reduced glutathione (GSH) protects the red cell membrane and haemoglobin from the deleterious effects of oxidation. [2, 3]

The G6PD enzyme deficiency belongs to a group of hereditary abnormalities and in this case, the activity of the erythrocyte G6PD enzyme is markedly diminished in the range of 8-20 percent of normal. The normal reference range being 65-150 percent.[2]

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The normal enzyme is designated as G6PDB. This represents the most common type encountered in all population groups. Among the persons of African descent, a mutant enzyme with normal activity known as G6PDA+ is prevalent. The African deficiency type is designated G6PDA-.[4, 5, 6]

The prevalence of G6PD deficiency varies widely from being very rare in the indigenous populations of Northern Europe to frequencies of about 20 percent in parts of Southern Europe, Africa and Asia; and up to 40 percent in some areas of Southern East Asia and the Middle East.[7, 8, 9]

G6PD enzyme deficiency affects an estimated 400 million people worldwide,[7, 8] an estimated 21 percent of the male population was reported to be G6PD deficient (G6PDA- type) in Nigeria.[7, 8, 10] This high frequency of G6PD Deficiency suggest that G6PD Deficiency confers a selective advantage in many population. Many studies have also shown that resistance to malaria could have accounted for this high frequency.[11]

Variable results had been published with regards to the association between G6PD deficiency and the development of jaundice in neonate. Almed et al reported 40 percent; Owa reported 62.3 percent; Sodeinde et al, reported 30.9 percent; while Uko et al, reported 38 percent.[12, 13, 14,15,16,17]

Haemolytic anaemia and hyperbilirubinaemia are the two major clinical consequences of G6PD enzyme deficiency. [13] In view of this fact, coupled with the frequent presentation of anaemia and jaundice amongst children in this environment, the idea of this study was conceived to determine the local prevalence of G6PD deficiency among children presenting with jaundice in Ilorin.

Materials and Methods

The study was carried out in the department of haematology, general out patients department and department of paediatrics, University of Ilorin Teaching Hospital, Nigeria. The subjects for this study included male and female children from one day to 15 years old, who had clinical evidence of jaundice. Subjects who were transfused in the previous 6 weeks and premature babies presenting with jaundice were excluded from this study.

Clearance was obtained from the Ethical Committee of the hospital. Informed consent was also obtained from the mothers of these children after adequate explanation and education of what the study entails.

Sample collection

One hundred children were recruited into the study conducted over a period of one year. Three (3) millilitres of blood sample was obtained from the ante cubital vein in infants and young children, and superficial vein on the dorsum of the hand in neonates, after adequate antiseptic preparation. This procedure was carried out by the paediatricians. The specimen was collected into specimen bottle containing ethylene diamine tetra acetic acid (EDTA) as anticoagulant. G6PD screening was carried out within 6 hours after collection. Other investigations done included Haemoglobin concentration, reticulocyte count, Hb electrophoresis and serum bilirubin (SB).

G6PD screening, reticulocyte counts and Hb concentration were repeated 6 weeks later for subjects who were G6PD deficient and had high reticulocyte count during the crisis period. The G6PD results considered were carried out post haemolytic period when subjects were in a stable state condition. The initial G6PD screening results obtained on first contact served as an additional control for subjects re-screened post crisis period and thus assisted further in categorizing subjects.

Methods

G6PD screening and status was determined by methaemoglobin reduction method of Brewer. [17, 18, 19] Hb determination was carried out using the sysmex auto analyser model KX 21 while reticulocyte count was carried out by visual method. [17] Hb electrophoresis was carried out only among subjects $\geq$ 6 months old.

Statistical Analysis

Data analysis was by the inferential statistical methods employing the chi-square tests and students t-test. The statistical significant of the data was based on p-value < 0.05. All data analysis was done on a computer statistical package with the EPI INFO version 6.0 software.

Results

Results of sixty-eight (68) males and thirty-two (32) females were analysed. The mean age of the subjects was 4.8(SD5.0) years. Table 1 shows the age distribution of subjects screened for G6PD. Of the one hundred subjects screened for G6PD Deficiency, the neonates formed the largest group while the pre-school Children formed the least populated group.

Table 2 shows the Mean values of Haemoglobin concentration and Reticulocyte count in G6PD deficient and G6PD normal subjects. The mean Hb for G6PD deficient subjects was 11.4g/dl (SD3.5) and 11.1g/dl (SD3.9) for G6PD normal subjects. The difference was not statistically significant (P = 0.76). The overall mean serum bilirubin for G6PD deficient subjects was 115µmol/l (SD87.6) and 97.8µmol/l (SD94.6) for G6PD normal subjects. The difference was not statistically significant (P = 0.350). Similarly, the mean reticulocyte count was 2.8% (SD1.9) among G6PD deficient subjects and 2.9% (SD3.9) in G6PD normal subjects. The difference was not statistically significant (P = 0.76).

Table 1: Status and age distribution of subjects screened for G6PD

Age Group	G6PD Deficient Subjects		Normal Subjects		Total
1 – 28 Days	13	34.2	25	65.8	38
1 – 5 Yrs	10	45.6	12	54.5	22
6 – 10 Yrs	13	68.4	6	31.6	19
11 – 15 Yrs	7	33.3	14	55.7	21
Total	43	43.0	57	57.0	100.0

Table 2: Mean values of Haemoglobin concentration and Reticulocyte count in G6PD deficient and G6PD normal subjects

Parameters	G6PD Deficient Subjects*	Normal Subjects*	P-Value
Hb (g/dl)	11.4 (3.5)	11.1 (3.9)	0.76
Reticulocyte count (%)	2.8 (1.9)	2.9 (3.9)	0.76
SB (µmol/l)	115.6 (87.6)	97.8 (94.6)	0.38

*Figures represent the mean (with SD in parentheses).

Table 3 shows Hb Electrophoresis pattern among subjects screened for G6PD. Thirty eight (38) subjects of the one hundred subjects were age < 6 months old and were excluded from Hb electrophoresis. Of the remaining sixty two (62) subjects, fourteen (14) were HbSS and only two (2) of the fourteen subjects with HbSS, were G6PD deficient. Table 4 shows status and sex distribution of subjects screened for G6PD. The prevalence rate is higher amongst Males than females.

The overall prevalence of G6PD deficiency among children studied was 43.0 [males (50 percent) and females (28.1 percent). In percentage prevalence of G6PD Deficiency subjects, stratified by age, there is a gradual increase

in the prevalence rate which peaked around the age group of six (6) to ten (10) years and gradually tapered. This is shown in Table 1 and Figure 1.

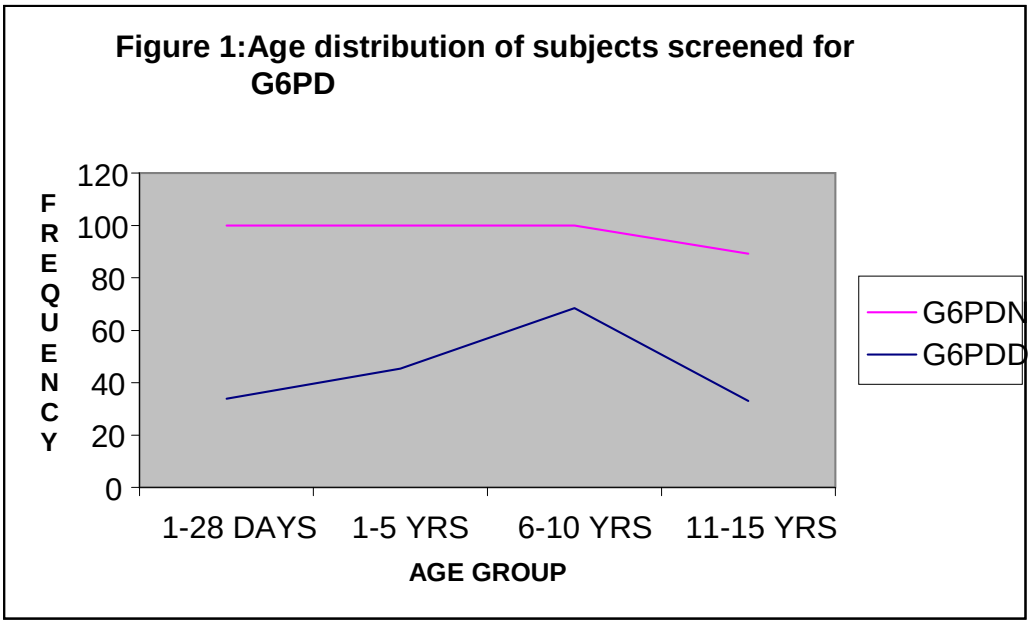

Table 3: Hb genotypes among 62 subjects screened for G6PD by electrophoresis

Status	G6PD Deficient Subjects*	Normal Subjects*	Total
AA	15 (68.2)	10 (25.0)	25
AS	4 (18.2)	15 (37.5)	19
SS	2 (9.1)	12 (30.0)	14
SC	1 (4.5)	3 (7.5)	4
Total	22 (100.0)	40 (100.0)	62

*Figures represent the absolute figures (with percentages in parentheses).

Table 4: Sex distribution of subjects screened for G6PD

Sex	G6PD Deficient Subjects		Normal Subjects		Total
	No	Percent	No	Percent	
Male	34	50.0	34	50.0	68
Female	9	28.1	23	71.9	32
Total	43		57		100.0

Discussion

Glucose-6-phosphate dehydrogenase deficiency is a major cause of severe anaemia among children in Nigeria with significant morbidity.[12] This is so because of the widespread indiscriminate use of oxidant agents in the course of treating malaria and other related conditions in children including some agents often used in neonates and infants in this environment. [14]

The overall prevalence of G6PD of 43.0 in this study group (jaundiced subjects) is twice the figure (21) obtained by Kehinde and Akinyanju in a study conducted among the healthy population subjects in Lagos [10]. This high prevalence obtained in this study is however comparable with that of Ahmed et al in Zaria; which was done among a similar group of subjects.[12] Likewise, the finding of 34.2 percent prevalence in neonates in this study is similar to studies by Sodiende et al[15], and Uko et al.[16]

This variation in figures might be attributed to differences in the study population rather than differences in geographical location. This study also highlighted the pattern of prevalence of G6PD deficiency among the various age groups. There is an indication of a gradual increase in the prevalence rate with the highest recorded in the age group of six (6) to ten (10) years. This might also be an indication that study conducted within or closer to this age group with jaundice might be associated with a high prevalence.

In this study, male subjects were much more affected than the female subjects. This thus further reaffirmed the natural history of G6PD deficiency of being an X-linked recessive disorder, and the fact that only male hemizygotes and female homozygotes are most often affected. Female heterozygotes who are G6PD deficient, acquired this through the phenomenon of normal X-chromosome inactivation of the Lyon-Hypothesis.[10]

The commonest presentations of patients with G6PD deficiency especially during the crisis period are recurrent haemolytic anaemia, low haemoglobin concentration and high reticulocyte count. It is possible therefore, that apparent G6PD normal subjects could have been G6PD deficient if screening test was conducted before a haemolytic crisis while also appearing G6PD normal in the immediate post haemolytic period. The explanation for this scenario is that the older red cells with least G6PD activity are selectively destroyed during haemolytic attack and the apparent increase in G6PD activity is further enhanced by reticulocyte response.[21]

In this study, only G6PD results during post haemolytic period when subjects were in a stable condition were considered. This is reflected in the mean Hb concentration of 11.4g/dl (SD3.5) for G6PD deficient subjects and 11.1g/dl (SD3.9) for G6PD normal subjects; and in the mean reticulocyte count of 2.8% (SD1.9) for G6PD deficient and 2.9% (SD3.9) for G6PD normal subjects. The bilirubin levels of 115.2µmol/l (SD87.6) for G6PD deficient subjects and 97.8µmol/l (SD 94.6) for G6PD normal was not statistically significant. Likewise, the bilirubin level in those with and without haemoglobinopathy was not statistically significant. It is important to conduct this screening using MRT in the post haemolytic period when high reticulocyte counts of crisis period have normalized. Conducting screening during post haemolytic period would significantly eliminate false positive results and erroneous high prevalence rate.

This study is limited by the qualitative method of methaemoglobin reduction screening test employed. This is in view of its sensitivity and specificity as well as the conflicting reports of its sensitivity as reported in some studies.[20] Methaemoglobin reduction screening test however remains a useful reliable alternative especially in developing countries like ours; where resources are limited and where cost of routine screening of G6PD is an issue.

Conclusion

The prevalence of G6PD deficiency among children presenting with jaundice in Ilorin is high. This figure therefore clearly indicates that there is a 43 percent chance for children presenting with jaundice in this age group in Ilorin, to have the underlying predisposition as G6PD deficiency. In view of the high prevalence rate of G6PD deficiency among jaundiced subjects in this study, screening for G6PD deficiency will be a very useful test in the differential diagnosis of jaundice in that age group. Screening for G6PD deficiency should therefore be integrated as part of the first line investigations for all children presenting with jaundice and / or anaemia especially in this age group.

This finding will also provide the health care givers the necessary information about the local prevalence, and the need to be more cautious on their choices of agents in order to avoid the complications of haemolysis in patients who are G6PD deficient. Also, this information would give the health care professionals the ground to establish counselling units within the hospital for parents of these children.

Future prevalence study of G6PD in this environment using quantitative method might be required to accurately determine the prevalence rate among jaundiced subjects.

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