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Glucose-6-Phosphate Dehydrogenase Deficiency in Children at Vwang Village, Vom, Jos South, Plateau State, Nigeria

IHEANACHO CHARITY[1, 2], ETUKA CHRISTIAN[1], UGWU BEN KINGSLEY[1], NNANNA OGBONNAYA[1]

[1]DEPARTMENT OF MEDICAL LABORATORY SCIENCE, UNIVERSITY OF JOS
[2]HEAMATOLOGY DEPARTMENT, JOS UNIVERSITY TEACHING HOSPITAL

Abstract: **Glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency), also known as favism (after the fava bean), is a sex (X) linked recessive inborn defect of metabolism that predisposes to hemolysis (spontaneous destruction of red blood cells) and resultant jaundice in response to a number of triggers, such as certain foods (fava beans), illness, or medication (ascorbic acid). Common among people of Mediterranean and African origin. The condition is characterized by abnormally low levels of glucose-6-phosphate dehydrogenase, an enzyme involved in the pentose phosphate pathway that is especially important in the red blood cell. G6PD deficiency is the most common human enzyme condition.; it is particularly common in populations living in malaria-endemic areas. This study was aimed at determining the prevalence of G-6-PD deficiency in children at Vwang Village, Vom, Jos South, Plateau State, Nigeria. 242 children consisting of 126(52.1%) males and 116(47.9%) females with age ranging from 1-12 years were screened for G-6-PD deficiency using the methaemoglobin reduction test. Of the 242 children screened, the overall prevalence was 52(21.5%) with 25(19.8%) males and 27(23.3%) females. The prevalence of G-6-PD deficiency was found to be high in females when compared to males, although there was no statistically significant difference (P>0.05) between G-6-PD deficiency in relation to gender. The highest prevalence rate of G-6-PD deficiency was observed among children in the age group of 1-4 years, however, not statistically significant (P>0.05). This study indicates a high prevalence of G-6-PD deficiency among children residing in Vwang Village, Vom, Jos South, Plateau State, Nigeria.**

Keywords: **Glucose-6-Phosphate Dehydrogenase Deficiency(G-6-PD), Children, Vom, Jos South, Plateau State.**

1. INTRODUCTION

1.1 Background of Study:

The red blood cell, an important cell in the human body is particularly prone to damage when it is exposed to certain external stimuli which affect its membrane causing its destruction in an individual who is deficient for the enzyme Glucose-6-Phosphate Dehydrogenase (G-6-PD).

Glucose-6-Phosphate Dehydrogenase (G-6-PD) is a cytoplasmic enzyme that is widely distributed in all cells of the body (1). Glucose-6-phospahte dehydrogenase (G-6-PD) catalyses the initial step in the pentose phosphate pathway of glycolysis (2). It is an enzyme in the Hexose Monophosphate Shunt that catalyses the oxidation of Glucose-6-Phosphate (G-6-P) to 6-phosphogluconate (6-PG) and concomitantly, Nicotinamide Adenine Dinucleotide Phosphate ($NADP^+$) is reduced to NADPH. The NADPH, a required co-factor in many biosynthetic reactions, maintains Glutathione (GSSG) in its reduced form (GSH). Reduced Glutathione acts as a scavenger for free radicals and thus helps reduce oxidized

haemoglobin to free haemoglobin, otherwise oxidized haemoglobin will precipitate as Heinz bodies. While many other body cells have other mechanism of generating NADPH, the red blood cells rely completely on G-6-PD activity because it is the only source of NADPH that protects the red cell against oxidative stress (3). The red cells are exquisitely sensitive to oxidative damage in the absence or reduced activity of G-6-PD as they lack other NADPH producing enzymes (1).

G-6-PD deficiency is the most common disease producing enzymopathy in man. It is inherited as an X-linked recessive disorder, affecting about 400 million people worldwide (3). The gene that codes for G-6-PD has a number of variants; some cause mild deficiencies and some severe deficiencies (4; 5). The gene is located on the X-chromosome, thus females can be homozygous or heterozygous but males can only be hemizygous for the gene. As a consequence and through lyonization (inactivation of one X-chromosome), heterozygous women have two red blood cell populations, each resulting from the expression of one of two G-6-PD alleles. One population may have normal or deficient G-6-PD level, whereas the other population may have another level of deficiency. G-6-PD variants are classified according to the severity of the G-6-PD deficiency based on the level of enzyme activity compared with normal activity in the population under consideration. Class I variants cause Congenital Non-Spherocytic Haemolytic Anaemia (<10% of normal activity), Class II variants cause severe enzyme deficiency (< 10% of normal activity), Class III variants cause moderate to mild enzyme deficiency (10 – 60 % of normal activity), Class IV variants cause very mild or no enzyme deficiency (60 – 100 % of normal activity) (6). The highest prevalence rates of G-6-PD deficiency occur in persons of African, Asian, Mediterranean or Semitic descent. Specific prevalence rates worldwide ranges from 3.9% in India, 12.8% in the USA and 50% in the Middle East (3). In Nigeria, the prevalence of G-6-PD deficiency ranges from 4 – 26% with the male population having about 20 – 26%, this prevalence rate varies from one community to another (1).

G-6-PD status is usually determined by measuring enzyme activity in haemolysate from whole red blood cells with either quantitative or qualitative assays (6). G-6-PD deficiency transmitted X-chromosomally can be detected reliably in homozygous female and hemizygous men with a number of tests. Diagnosing G-6-PD deficiency in heterozygous women is difficult and a large part of this group is missed, as a result of lyonization, the cytochemical assay is the only reliable assay to discriminate between heterozygous- deficient women and non- deficient women or homozygous women (4; 5).

G-6-PD deficiency contributes to neonatal jaundice which is accompanied by hyperbilirubinaemia and put infants at risk for kernicterus within the first few days of life. Kernicterus can lead to hearing deficits, mental problems and permanent neurologic damage. During childhood, many children with G-6-PD deficiency are healthy until they are exposed to a pro-oxidant medication or chemical. Classically, antimalarial drugs are strong pro-oxidants and have substantial use in Sub-Saharan Africa. Additionally, exposure to the pro-oxidant Naphthalene, the active ingredient in mothballs is common among young children. In G-6-PD deficiency, pro-oxidant exposure can lead to a rapid imbalance in the redox state in red blood cells leading to haemolysis and resultant severe anaemia, heart failure and even death if not recognised early (7). Haemolysis is induced by sudden destruction of the older and more enzyme deficient erythrocytes. This occurs after exposure to some drugs of high redox potentials, mothballs, henna, Fava beans or following certain infections and metabolic activities (8). This study is aimed at determining the prevalence of G-6-PD deficiency in children at Vwang Village, Vom, Jos South, Plateau State, Nigeria.

1.2 Justification:

G-6-PD deficiency which is a life threatening disorder affecting millions of people around the world causes haemolytic anaemia in most of the persons that are deficient for the enzyme (G-6-PD), the significance of the study is to know the G-6-PD status of children at Vwang Village, Vom, Jos South so as to help advice the parents/guardian of G-6-PD deficient child of the effects if such child is exposed to the oxidant products. The likely danger to the children if this research is not carried out is that the parents might not know that their children are G-6-PD deficient and if s/he is deficient, they will know the oxidant materials to avoid so as to avert the consequence caused by the enzyme deficiencies which is haemolytic anaemia, and if not detected on time will lead to other complications and the eventual death of the child.

2. MATERIALS AND METHODS

2.1 Study Area:

The study was conducted in Vwang Village which is one out of the four (4) wards of Vwang district. Vwang district comprises four (4) wards namely Vwang, Turu, Fwil, and Chugwi. Vwang ward is located in Vom which is situated about

38km south of Jos, with Vom having a Latitude of 9°43'60" N, Longitude of 8°46'60" E in DMS (Degrees Minutes Seconds) with an Altitude of 1370 above sea level. The major ethnic group in this community is Berom. Other minor settlers are the Igbos, Irigwi, Mwaghavul, Tarok, Ngas among others. The major occupation of the population is both subsistence farming as well as commercial farming of Acha, Irish potatoes, Millet and Bennie seed.

2.2 Method for Blood Sample Collection:

Each child was made to sit comfortably on a chair. A tourniquet was applied at the upper arm to make the veins prominent. The area around the antecubital fossa was sterilized using cotton swab moistened with 70% alcohol. With the aid of sterile 5ml syringe and needle, 2ml of blood was withdrawn into the EDTA plastic sterilin container and gently mixed. The blood sample was transported in an ice pack to the Haematology laboratory of the Jos University Teaching Hospital for the assay.

2.3 LABORATORY PROCEDURES:

2.3.1 *Methaemoglobin Reduction Test (9):*

2.3.2 Reagents used:

a. Sodium Nitrite ($NaNO_2$)-180mmol/

Dextrose -280mmol/L

b. Methylene blue-0.4mmol/L

The blood was tested within 8 hours of collection.

2.3.3 Method :

I. 3 small *glass* tubes (13 x 100mm, inside diameter 11mm) were labeled *Test*, *Normal*, *and Deficient.*

II. Into each tube were pipetted the following as shown in the table 2.1 below.

III. The tubes were stoppered and gently mixed. All three samples were incubated in a water bath at 37^{O}C for 90minutes.

IV. 3 large tubes (16 x 150mm, inside diameter 14mm) were labeled as described in step 1 above. 10 ml of distilled water was pipetted into each tube.

V. 0.1ml of the well mixed sample from the *Test*, *Normal*, and *Deficient* tubes was transferred to the large tubes containing distilled water, the contents of each tube was gently mixed.

VI. The colour of the solution in each tube was then examined macroscopically.

Table 2.1: PROTOCOL TABLE FOR METHAEMOGLOBIN REDUCTION TEST

Tubes	**Test**	**Normal control**	**Deficient control**
Sodium nitrite-glucose reagent(Fresh)	0.05ml	_	0.05ml
Methylene blue-reagent	0.05ml	_	_
Donors whole blood	1ml	1ml	1ml

2.3.4 Interpretation of Test Results:

NORMAL G-6-PD ACTIVITY: the colour of test solution similar to that of the red colour of normal control tube; therefore the test is negative for G-6-PD deficiency with the individual having a normal G-6-PD activity.

G-6-PD DEFICIENCT SAMPLE: the colour of test solution similar to the brown colour of deficient tube, therefore the test is positive for G-6-PD deficiency i.e the individual is G-6-PD deficient.

HETEROZYGOUS STATE: Results from a heterozygote were midway between normal G-6-PD activity and G-6-PD deficient homozygote.

3. RESULTS

Table 3.1: Prevalence of G-6-PD Deficiency in Children

G-6-PD Status	Frequency	Percentage (%)
Normal	190	78.5
Hemizygous	25	10.3
Heterozygous	21	8.7
Homozygous	6	2.5
Total	242	100.0
Normal	190	78.5
Deficiency	52	21.5
Total	242	100.0

Table 3.2 above shows the prevalence of G-6-PD deficiency in children. A total of 242 children recruited into the study shows that 52(21.5%) were G-6-PD deficient, 21(8.7%) were diagnosed heterozygous for G-6-PD deficiency, 6(2.5%) were diagnosed homozygous for G-6-PD deficiency, 25(10.3%) were diagnosed hemizygous and 190(78.5%) had normal G-6-PD activity.

Table 3.2: Prevalence of G-6-PD Deficiency in Relation to Age Group

Age group	**G-6-PD Status**	
	Normal	**Deficient**
1-4	21(65.6%)	11(34.4%)
5-8	86(78.2%)	24(21.8%)
9-12	83(83.0%)	17(17.0%)
Total	190(78.5%)	52(21.5%)

P-value = 0.114

The prevalence of G-6-PD deficiency in relation to age group is presented in table 3.3 above. Age group of 1-4 years had the highest prevalence of G-6-PD deficiency of 34% while age group of 9-12 years had the lowest prevalence rate of G-6-PD deficiency of 17.0% with P-value of 0.114 which showed that there was no statistical significant difference between G-6-PD deficiency in relation to age groups.

Table 3.3: Prevalence of G-6-PD Deficiency in Relation to Gender

Gender	**G-6-PD Status**		
	Normal	**Deficient**	
Male	101(80.2%)	25(19.8%)	
Female	89(76.7%)	27(23.3%)	
Total	190(78.5%)	52(21.5%)	

P value = 0.516

The table above shows the prevalence of G-6-PD deficiency in relation to gender. Female gender had the highest prevalence rate of 23.3% when compared with the male with 19.8% with P-value of 0.516 which showed that there was no statistical significant difference between G-6-PD deficiency in relation to genders

4. DISCUSSION

This study aimed at determining the prevalence of G-6-PD deficiency in children at Vwang village, Vom, Jos South, Plateau State Nigeria. The overall prevalence of G-6-PD deficiency in this study was found to be 21.5% and this falls within the range (4-26%) reported in Nigeria (1). The prevalence rate of this study is higher than the study carried out in Southwestern Nigeria on prevalence of glucose-6-phosphate dehydrogenase deficiency in Nigerian children of different ethnic groups, where 1,122 children were screened for the enzyme deficiency with a prevalence rate of 15.3% being recorded (7). The high prevalence rate of G-6-PD deficiency in this study could be as a result of environmental factor

where malaria parasite is highly endemic in this region and as a result of consanguineous marriage that was being practiced by their ancestors hence this may have influenced the genetic makeup and resulted in the propagation of such deleterious genes among the population (10).

The high frequency of occurrence of G-6-PD deficiency in Nigeria is because malaria parasite (*Plasmodium falciparum*) is endemic in Nigeria and hence G-6-PD deficiency plays a protective function against malaria parasite (7).

In this study, the prevalence of G-6-PD deficiency in relation to age group was found to be high in the age group of 1-4 years with a prevalence rate of 34.4% while the lowest prevalence rate was observed in the age group of 9-12 years, although no significant difference between G-6-PD deficiency in relation to age group was observed.

The overall prevalence of G-6-PD deficiency in relation to gender was found to be high in females (23.3%) when compared to males (19.8%). The findings in this study is contrary to the findings done by other researchers where males usually had the highest prevalence and as it would be expected of an X-linked disorder where the enzyme deficiency occur more in the males than in the females because the males only have one X-chromosomes (3) when compared to the females that have two X-chromosomes (11).

G-6-PD deficient females could either be homozygous or heterozygous. The heterozygous deficient females have a mixed population of erythrocytes owing to the random inactivation of one of the two X-chromosomes known as Lyonization where one of the erythrocyte populations is G-6-PD deficient and the other has a normal G-6-PD activity (12). In geographical region where the frequency of G-6-PD deficient allele is high, homozygous females are not rare (11) and this was the finding in this study where 6 female children were diagnosed homozygous for the G-6-PD gene.

In this study, 19.8% of the male population is deficient for the enzyme and this is similar to the study carried out on Nigerian males resident in Jos where the prevalence rate was found to be 20% (1). There was however no significant difference between G-6-PD deficiency in relation to gender.

The high prevalence rate of G-6-PD deficiency in females when compared to males may however not be explained but this could serve as a ground for further research to disprove this fact.

5. CONCLUSION

Within the limits of experimental error, it can thus be concluded that the prevalence of G-6-PD deficiency in the study was 21.5% and this shows a high prevalence rate hence the notion that malaria parasite plays an important role in the protection against G-6-PD deficiency is now widely accepted because malaria parasite is highly endemic in this part of the world.

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