

*Full Length Research Paper*

## Incidence of glucose-6-phosphate dehydrogenase deficiency in anaemic patients attending General Hospital Kafanchan, Kaduna State, Nigeria

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**Glucose-6-phosphate dehydrogenase (G-6-PD) deficiency is one of the most well known human genetic defects and could possibly result in acute haemolysis after exposure to various oxidative conditions. This work was therefore carried out to determine the incidence of G-6-PD deficiency in anaemic patients attending General Hospital Kafanchan, Kaduna State, Nigeria. The study group comprised of 50 sickle cell, 60 iron deficient and 40 malaria patients, while 50 apparently healthy individuals served as control. Statistical analyses of the results according to age group, sex, marital status, packed cell volume (PCV) values, G-6-PD activities and genotype revealed 24 (12%), 26 (13%) and 6 (3%) were G-6-PD deficient in sickle cell, iron deficiency anaemia and apparently healthy, respectively. G-6-PD deficiency was absent in all malaria patients screened. In terms of marital status, singles of both males and females recorded higher deficiency than their married counterpart ( $P < 0.05$ ). Furthermore, the age interval of 0 to 10 years old recorded highest number of G-6-PD deficient subjects in all the anaemic patients ( $P < 0.05$ ). The study therefore suggests the need for routine G-6-PD screening test on anaemic patients to avoid factors which could further precipitate haemolytic crisis.**

**Key words:** Incidence, glucose-6-phosphate dehydrogenase (G-6-PD), anaemia, haemolysis, Kafanchan, Nigeria.

### INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) enzyme catalyzes the first step in the pentose phosphate

pathway, leading to production of antioxidants that protect cells against oxidative damage (Luzzatto et al.,

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**Table 1.** G-6-PD Incidence in the total population screened.

G-6-PD Status	Sickle cell	Iron deficient	Malaria	Apparently healthy
	No. (%) of Subjects	No. (%) of Subjects	No. (%) of Subjects	No. (%) of Subjects
Normal	6 (3)	7 (3.5)	27 (13.5)	33 (16.5)
Reduced	20 (10)	27 (13.5)	13 (6.5)	11 (5.5)
Deficient	24 (12)	26 (13)	0 (0)	6 (3)

2001). G6PD deficiency is the most common enzymatic erythrocyte disorder which is linked to the X-chromosome in humans (Elyassi and Rowshan, 2009; Valaes et al., 1998). A G6PD-deficient patient lacks the ability to protect red blood cells against oxidative stresses produced by the administration of certain drugs, metabolic conditions, infections and ingestion of some foods (Cappellini and Fiorelli, 2008; Glader, 2008).

Deficiency in G-6-PD is believed to affect about 100 million people globally (Carter et al., 2002) and the rate of prevalence is higher among Africans and Asian (Abdulrazzaq et al., 1999). Reports showed that the G6PD A- allele, which contains two mutations, A376G and G202A, is the most common G6PD deficiency variant in Africa (Howes et al., 2013; Johnson et al., 2009) and the severity resulting from G-6-PD deficiency varies significantly between races with more severe deficiency occurring in the Mediterranean population and the milder form in the African population (Owa and Osanyituyi, 1988). Several reports have been published on this genetic disorder in various geographic populations (Beutler, 1993). It has been reported in Greece (Stamatoyannopolous, 1971), Romania (McCurdy et al., 1972), Algeria (Nafa et al., 1994), United State (Geskin et al., 2001), Saudi Arabia (Abdulrazzaq et al., 1999) and Nigeria (Abubakar et al., 2005).

In Nigeria, G6PD deficiency occurs in 24% of boys and 5% of girls (Ademowo and Falusi, 2002). It is also known to be a significant cause of anaemia in children, especially neonates (Sodeinde et al., 1995). Yoruba children had the highest prevalence (16.9%) of G6PD deficiency followed by Igede children (10.5%) and children of Igbo (10.1%) and Tiv (5.0%) ethnicity. Igbo children had 0.38 times the odds of being G6PD deficient compared to Yoruba children. The odds for Igede and Tiv children were not significantly different from Yoruba children (Williams et al., 2013).

Haemolytic anaemia due to G-6-PD deficiency could be severe and life threatening (Luzzatto and Testa, 1978). About 25% of adults throughout the country have the sickle cell trait, AS, while the Hb C trait is largely confined to the Yoruba people of southwestern Nigeria in whom it occurs in about 6%. Other variant hemoglobins including beta thalassaemia are rare, but alpha thalassaemia occurs in 39% (32% with 3 alpha-globin genes; 7% with 2 alpha-globin genes) (Akinyanju, 1989). While screening of patients for G-6-PD deficiency is not a common practice

in health-care delivery services of most poor African countries, there is a need for regular screening of individuals particularly malarial and anaemic patients to be able to establish their G-6-PD status. This is to avoid receiving drugs that could further precipitate haemolytic crisis in G-6-PD deficient individuals.

## MATERIALS AND METHODS

### Study subjects

This study was carried out on a total of 150 anaemic patients attending general Hospital Kafanchan, Kaduna State, North-Central Nigeria. The patients consist of 50 sickle cell anaemia, 60 Iron deficient anaemia and 40 Malaria patients while 50 apparently healthy individuals served as control. 113 of the subjects were females and 87 were males selected on age ranging from 0 to 75 years old.

### Sample collection and analysis

The blood samples (5 ml) from each subject were collected through venepuncture from the antecubital vein of the forearm into dipotassium ethylene diaminetetracetic acid containers. The collected samples were screened immediately for G-6-PD using methaemoglobin reduction test (Brewer et al., 1962), serum ferritin radioimmunoassay test was used in the determination of iron deficiency. Malaria test strips were used to confirm malarial infection in the study group, genotype screening was used to confirm the sickle cell (SS) status of the studied group not under blood transfusion, while packed cell volume (PCV) of all the sampled patients was determined using microhaematocrit reader. The data were subjected to statistical analysis.

## RESULTS

The results obtained are presented in Tables 1 to 5. The values are classified on the basis of sex, marital status, PCV values, G-6-PD activity and genotype.

## DISCUSSION

The overall incidence of G-6-PD deficiency in the total population sampled has shown that Iron deficiency anaemic patients recorded highest prevalence while no deficiency was recorded among the malaria patients screened. The NADPH, a required co-factor in many biosynthetic reactions, maintains glutathione in its reduced

**Table 2.** Relationship between G-6-PD deficiency and marital status.

Status	Sickle cell		Iron deficiency		Apparently healthy	
	Total subjects	Deficient subjects (%)	Total subjects	Deficient subjects (%)	Total subjects	Deficient subjects (%)
Married male	5	5(10)	6	5(8.3)	4	1(2)
Single male	20	18(36)	13	11(18.3)	23	4(8)
Female married	4	4(8)	18	18(30)	5	4(8)
Single female	21	13(26)	23	20(33.3)	18	8(16)

**Table 3.** The relationship between G-6-PD and sex.

Group	Sickle cell		Iron deficiency		Apparently healthy	
	Male n=(25)	Female n=(25)	Male n=(19)	Female n=(41)	Male n=(27)	Female n=(23)
Normal	2(8)	8(32)	3(15.8)	3(7.3)	22(8.1)	11(47.8)
G-6-PD deficient	23(92)	17(68)	16(84.2)	38(92.7)	5(18.5)	12(52.2)
Homozygote	-	7(41.2)	-	14(36.8)	-	4(33.3)
Heterozygote	-	10(58.8)	-	24(63.2)	-	8(66.7)

**Table 4.** Relationship between G-6-PD deficiency and age of subjects.

Age group (years)	Sickle cell		Iron deficient		Apparently healthy	
	Total subject	Deficient subject	Total subject	Deficient subject	Total subject	Deficient subject
0-10	39	35	28	23	10	-
11-21	2	2	4	4	16	5
22-32	4	4	15	15	15	6
33-43	3	2	16	8	2	1
44-54	2	2	4	4	5	4
≥55	-	-	1	1	2	1

**Table 5.** Relationship between PCV and G-6-PD deficiency.

Group	Sickle cell		Iron deficiency		Apparently healthy	
	PCV (%)	No. of def. Subjects	No. of def. Subjects	No. of def. Subjects	No. of def. subjects	No. of def. subjects
23-28		29		45		-
29-34		15		8		-
35-40		-		-		11
41-46		-		-		2
47-53		-		-		4

reduced form. 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 mechanisms of generating NADPH, the red blood cells rely completely on G6PD activity because it is the only source of NADPH

that protects the cell against oxidative stress (Obasa et al., 2011).

Iron deficiency anemia is the most common form of anemia. Iron deficiency causes approximately half of all anemia cases worldwide, and affects women more often than men (Stoltzfus, 2001). Iron is a key part of red blood cells. Without iron, the blood cannot transport oxygen

effectively. One means of losing iron is through bleeding. There are various ways of losing iron which include heavy, long, or frequent menstrual periods in women, cancer in the esophagus, stomach, small bowel, or colon, esophageal varices, usually from cirrhosis, the use of aspirin, ibuprofen, or arthritis medicines for a long time, which can cause gastrointestinal bleeding and peptic ulcer disease (Wikipedia). Consequently, the higher incidence of G6PD deficiency was recorded in females with iron deficiency and therefore anaemia will be more severe in women than men.

Although most cases of iron-deficiency anaemia are mild and rarely cause complications, additional effect of G6PD deficiency might trigger severe anaemia, since iron can be converted to radicals which could result to oxidative damage of the erythrocyte's membrane (Beutler, 1994) contributing to abnormal red blood cell breakdown.

Sickle cell anaemic patients recorded the highest prevalence, the sickle cell morphology already predetermines their dysfunctional capacity, with G-6-PD deficiency however, there is an additional stress to this group of patients since the free radical generated either by a parasitic infection or administration of offensive drugs can destroy some of the circulating normal red blood cells.

The absence of G6PD deficiency in malaria patients is not surprising as haemolysis affects mature red blood cells more readily as there are fewer of them to host malaria parasites (Stephen et al., 1986). Moreover, malaria parasites could not thrive in immature red blood cells, thus, when an infected RBC dies before the parasite is ready, the malaria parasite dies as well (Stocker et al., 1985) thereby inhibiting the chances of exerting a disease state and subsequent manifestation of typical symptoms. The study is also in agreement with the *in vitro* work of Capellini and Fiorelli (2008) who reported that malaria parasites grow slowest in G6PD-deficient cells. However, since malaria still sequesters in the liver, affected persons could become very ill from haemolysis and G6PD patients are contraindicated to anti-malaria. The higher prevalence of G6PD-deficiency in subjects of 0 to 10 years is alarming since G6PD deficiency predisposes neonates to neonatal jaundice and sensitivity to certain drugs. Also, untreated neonatal jaundice may lead to hidden risk for Kernicterus (Kaplan and Hammerman, 2004). There is therefore a need to pay special attention to this age group which are selected by the Padiatrics.

The higher incidence recorded in male subjects correlates with the established fact being X-linked, G6PD deficiency allele confers a selective advantage (Allison, 1960) though genetic heterogeneity may result in varying degree of haemolysis across individuals. However, the proportion of female subjects recorded in this study gives room for concern due to possible unfavourable lyonisation, where random inactivation of an X-chromosome in certain cells creates a population of G6PD-deficient red blood cells (Beutler, 1993; 1962; Beutler et al., 1962).

Also G-6-PD is known to generate reduced glutathione (GSH) which are free radical scavengers, however due to the deficiency of G-6-PD, the ability to generate GSH from its oxidized form (GSSG) is lost (Beutler, 1994), thus worsening the anaemia. This observation also correlates with higher number of iron deficient anaemic patients having lowest PCV value as compared to sickle cell anaemic patients.

## Conclusion

Incidence of G-6-PD deficiency is higher in the iron deficient and absent in malaria patients. Therefore, there is a need for screening anaemic patients as part of the overall health and welfare service to avoid further complications.

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## Conflict of interest

The authors declared no conflict of interest.

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