Original Research

Incidence of Glucose-6-phosphate dehydrogenase deficiency in anemic women attendigng the Colonial War Memorial Hospital in Suva, Fiji.

Brijesh Kumar,
Fiji School of Medicine
Suva
E-mail: b.kumar@fsm.ac.fj

Abstract

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzyme deficiency affecting over 400 million people worldwide, 90% of which are males. The deficiency is more common in areas that are or have been endemic for malaria as well as in populations originating from these sources. Neonatal jaundice and acute hemolytic anemia are the common clinical manifestations.

In Fiji both the major ethnic groups (Fijians and Indians) originated from areas where malaria was endemic. While malaria has never been endemic in Fiji there is a high prevalence of anemia in Fiji especially in females. This study attempted to determine if G6PD deficiency was the underlying cause of anemia in antenatal mothers. Blood from a total of 400 antenatal anemic mothers with Hb less then 10g/dL were collected and analyzed for G6PD deficiency using methemoglobin reduction test.

Two positive cases were identified; one was Indian while the other was Fijian indicating G6PD deficiency is not the underlying cause of the high incidence of anemia present in Fiji. This low prevalence of G6PD deficiency is consistent with a study in 1972 which revealed a prevalence of 0.11% and 1.23% in Fijians and Indians respectively. These results further confirm the theory that selection for G6PD deficiency occurs in presence of endemic malaria.

Introduction

The cytoplasmic enzyme Glucose-6-phosphate dehydrogenase (G6PD) while catalyzing the first step of the pentose phosphate pathway produces Nicotinamide Adenine Dinucleotide Phosphate (NADPH). NADPH takes part in various metabolic pathways including the regeneration of the reduced form of glutathione (GSH) as well as in maintaining the stability of the enzyme catalase. Both catalase and GSH are required for the detoxification of hydrogen peroxide. As pentose phosphate pathway is the main source of NADPH in red blood cells (RBC), a deficiency in G6PD would render RBC very susceptible to oxidative stress.

The G6PD gene consisting of 13 exons is located on band Xq28 on chromosome X while the DNA region upstream of the transcription initiation site is similar to that of other house keeping genes[1]. G6PD deficiency is genetically heterogeneous with about 400 variants listed on the basis of biochemical characteristics[1].

Majority of individuals with G6PD deficiency are unaware of their abnormality as they remain asymptomatic. Acute hemolysis being the most common clinical manifestation usually remains undetected as it may be rapidly compensated. Even so G6PD deficiency can cause clinical syndromes like Drug-induced hemolysis, Infection-induced hemolysis, Favism, Neonatal jaundice and Chronic nonspherocytic hemolytic anemia[1].

400 million people world wide are estimated to be affected by G6PD deficiency thus making it the most common enzymopathy [1,2]. Prevalence of G6PD deficiency is greater in tropical Africa, tropical and subtropical Asia, some areas of the Mediterranean and Papua New Guinea[1].

G6PD deficiency is more common in areas that are or have been endemic for malaria as well as in populations originating from these sources. Both the major ethnic groups (Fijians and Indians) originated from areas where malaria was endemic[3]. Also with the observation that anaemia is common in Fiji especially during pregnancy it was decided to determine if G6PD deficiency was the underlying cause of anaemia observed during pregnancy in Fiji.

Materials & Methods

A total of 400 blood specimens with Hb levels lower then 10 g/dL were selected from CWMH antenatal clinic during 2003 and 2004. These samples were screened for G6PD deficiency using the Methemoglobin reduction test (MRT)[4,5]. This is a coloric reaction using sodium nitrite and methylene blue chloride reaction. Sodium nitrite converts haemoglobin to methaemoglobin but when incubated with methylene blue there is stimulation of pentose phosphate pathway in normal subjects thus reducing methaemoglobin resulting in a clear

red colour. While in G6PD deficient samples the pentose phosphate pathway is inhibited therefore methaemoglobin is not reduced resulting in a dark brown colour.

Of the two readily utilized methods for screening G6PD deficiency the classical haematological test MRT was used in this study instead of the WHO recommended G6PD activity assay.

MRT being a qualitative screening test has a lower sensitivity (85%) then that of G6PD activity assay (100%) as expected, however the specificity for both tests are high (98-100%)[6]. Despite this MRT was selected for this study as it is more cost effective. Using basic medical economic analysis it was recently reported that MRT cost USD 0.15 while G6PD activity assay cost USD2.67[7].

Results and Discussion

For this study antenatal patients with haemoglobin below the normal range (11.5-16g/dL) were selected. Out of the 400 antenatal mothers selected 250 had Hb in 9-9.9g/dL range, 99 were in 8-8.9g/dL range, 33 were in 7-7.9g/dL range and 18 were in 6-6.9g/dL range as illustrated in Figure 1.

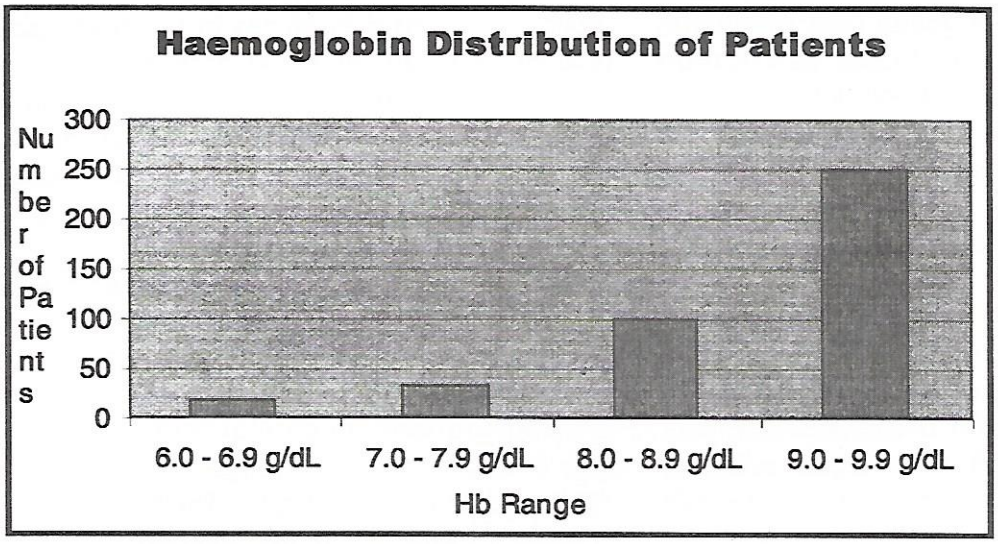

Figure 1. Haemoglobin distribution of patients.

Of the 400 patients screened only two were positive for G6PD deficiency. Both were from 2003 with Hb levels of 6.3g/dL and 6.7g/dL. Only 0.5% of the patients being positive indicate, anemia in pregnant mothers is probably not due to G6PD deficiency.

This result is not surprising as G6PD deficiency is inherited in a characteristic X-linked pattern implying it will be rare to find homozygous females. Although G6PD deficiency in terms of clinical expression is referred to as X-linked recessive, it is not truly recessive as heterozygous females can develop hemolytic attacks. This can be explained in terms of the coexistence of two cell population (G6PD+ and G6PD-) in heterozygotes as a result of X-chromosome inactivation.

The low prevalence of G6PD deficiency in this study is consistent with a study conducted in 1972 where a low prevalence was also discovered in both Fijian (0.11%) and Indian (1.2%) males[8]. Results of both of these studies confer with the hypothesis that G6PD deficiency is selected for in presence of endemic malaria. When the geographic distribution of G6PD deficiency is compared with the epidemiologic map of *Plasmodium falciparum* malaria this relationship is easily visualized [1].

It is also thought that G6PD deficiency confers resistance to *Plasmodium falciparum* malaria. A number of studies have been conducted to determine the mechanism of G6PD deficiencies protection against malaria. These have revealed that malaria growth is impaired in G6PD deficient cells especially in response to oxidative stress. More recently it has been shown that macrophages phagocytosised parasitized G6PD deficient red blood cells at an earlier stage when compared to parasitized normal G6PD red blood cells[9].

References

1. Luzzatto L, Metha A, Vulliamy T 2001, 'Glucose 6-phosphate dehydrogenase deficiency in *The Metabolic and Molecular Basis of Inherited Diseases*', edited by C Scriver, A.L Beoviolet, D Valle, W.S. Sly eds, 8th edition, volume 3, McGraw Hill, pp 4517-4553.

2. Wajcman H, Galacteros F 2004, 'Glucose 6-phosphate dehydrogenase deficiency: a protection against malaria and a risk for hemolytic accidents', *C R Biol,* vol. 327 (8), pp711-720.

3. Derrick RA, 1950, 'A history of Fiji' Govement Press, Suva.

4. Brewer GJ, Tarlov AR, Alving AS 1960, 'Methemoglobin reduction test – a new, simple in vitro test for identifying primaquine sensitivity' *Bulletin of the World Health Organization*, 22: pp 633-640.

5. Roper D, Layton M, Lewis SM 2001, 'Investigation of the hereditary haemolytic anaemias: membrane and enzyme abnormalities in *Practical Haematology'* Lewis S M, Bain B J, Bates I eds 9th edition, Churchill Livingstone, pp180-181

6. Sanpavat S, Nuchprayoon I, Kittikalayawong A, Ungbumnet W 2001, 'The value of methaemoglobin reduction test as a screening test for neonatal glucose 6-phosphate dehydrogenase deficiency', *J Med Assoc Thai* vol84 (suppl 1), pp S91-S98.

7. Wiwanitkit V 2005, 'Is the G6PD activity assay more cost effective than the methaemoglobin reduction test in screening for G6PD deficiency?', *Haema*, vol.8(1), pp 61-63.

8. Buchanan JG, Wilson FS, Nixon A D 1973, 'Survey for Erythrocyte Glucose-6-Phosphate Dehydrogenase Deficiency in Fiji', *The American Journal of Human Genetics*, Vol. 25. pp 36-41.

9. Cappadoro M, Giribaldi G, O'Brien E, Turrini F, Mannu F, Ulliers D, Simula G 1998, 'Early phagocytosis of glucose-6phosphate dehydrogenase (G6PD) deficient erythrocytes parasitized by may explain malaria protection in G6PD deficiency', *Blood* 92: 2527