FREQUENCY OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY IN ASYMPTOMATIC PAKISTANI POPULATION

Aamer Mehmood, Mohammad Akhtar*, Muhammad Farooq Khan Niazi**

CMH Rawalpindi, *PAF Base Masroor, **PNS Shifa Karachi

ABSTRACT

Objective: To determine the frequency of G6PD deficiency in asymptomatic Pakistan population.

Study Design: Cross sectional study.

Place and Duration of study: This was carried out at Pakistan Air Force (PAF) Hospital at PAF Base Masroor Karachi between June 2004 - September 2007

Patients and Methods: Healthy young males and females between the ages of 13 to 28 years were tested for G6PD deficiency. None of the individuals had the findings of chronic hemolytic anemia. Their test was carried out on Trinity Biotech visual, qualitative, colorimetric procedure for determining G6PD deficiency using dichlorophenol indophenols as an indicator.

Results: During the study period 888 individuals, 804 males and 84 females were tested for G6PD deficiency. Forty (4.5%) individual had G6PD deficiency. All were otherwise healthy with normal general physical examination, complete blood count, blood glucose level, liver function tests, renal function tests, lipid profile, urine analysis, electrocardiogram and X- Ray chest .Out of 804 males 40(5.0%) had G6PD deficiency. None of the 84 females had the enzyme deficiency.

Conclusion: G6PD deficiency is observed to be 4.5%.Our findings are in conformity with W.H.O data for geographic distribution of G6PD deficiency in Pakistan .It should be considered in the differential diagnosis of hemolytic anemia, especially following drug administration.

Keywords: Glucose-6-phosphate dehydrogenase, G6PD.

INTRODUCTION

G6PD is the most common congenital enzymopathy with a world wide distribution. World Health Organization has mapped the frequency of G6PD deficiency throughout the world with the highest rates of up to 26% of the general population in Middle East and Central Africa and the lowest <0.5 % in Northern Hemisphere including North Europe, UK, Scandinavian countries, Russia. and northern China. The frequency quoted in Pakistan is between 3-6.9% along with Southern China and Southern Russia i.e the areas adjoining Pakistan (Figure) [1]. The deficiency of the enzyme leaves the Red blood Cells more susceptible than normal to oxidative damages due to infections, fava beans and a number of drugs. The individual is asymptomatic even with the G6PD level of 20 % of the normal, but is extremely vulnerable of episodes of hemolytic anemia when exposed to severe infections but most importantly to commonly prescribed medicines like antimalarials, sulphonamides, analgesics, antihelmenths and antibacterial. In Pakistan, where all types of medicines can be purchased over the counter without any prescription, these drugs can lead to serious health impairment in the G6PD deficient individuals.

Objective

To determine the frequency of G6PD deficiency in asymptomatic Pakistan population.

PATIENTS AND METHODS

This cross sectional study was carried out at the clinical lab of PAF Hospital Masroor between June 2004 to Sep 2007 The individual, males and females, tested were asymptomatic between the ages of 13 years and 28 years from all over Pakistan. All the individuals were healthy candidates who reported for the enrolment in the Air Force, had normal general physical examination, none of them had the findings suggestive of chronic hemolytic anemia. Their test was carried out on Trinity Biotech visual, qualitative, colorimetric procedure for determining G6PD deficiency using dichlorophenol indophenols as an

Correspondence: Lt Col Aamer Mehmood, Classified Pathologist, CMH Rawalpindi
Email: mir_aamer@hotmail.com
Received: 24 July 2008; Accepted: 22 Jan 2009

indicator. All the subjects had normal blood complete picture, liver function test, renal function test, urine analysis, ECG, X –Ray chest and lipid profile and general physical examination.

RESULTS

During the study period 888 individuals, 804 (90.5%) males and 84 (9.5%) females were tested for G6PD deficiency. All had normal blood counts, blood glucose level, liver function tests, renal function tests, lipid profile, urine analysis, electrocardiogram and X- Ray chest. Out of 888 individuals 40 (4.5%) had G6PD deficiency. Out of 804 males 40 (5.0%) had G6PD deficiency. None of the 84 females had the enzyme deficiency.

DISCUSSION

G6PD deficiency is said to be the most common enzyme deficiency in the world affecting almost 400 million people globally. African, Middle Eastern and South Asian population are affected the most. Patients are males due to X linked pattern of inheritance, but female carriers can be clinically affected due to lionization where random inactivation of X chromosome in certain cells creates a population of G6PD deficient cells coexisting with the normal population1. G6PD is a dimeric enzyme of a single polypeptide chain of about 59 to the telomeric region of X chromosome very near the factor VIII (band Xq 28) [2]. The gene has been cloned and sequenced. It is known by cloning the gene that G6PD deficiency results from a variety of mutant alleles of it's structural genes. About 140 mutations have been described, most are single base changes leading to amino acid substitution [3]. Only two designated variants, G6PD A- and G6PD Mediterranean cause most significant hemolytic anemia [4, 5]. The high frequency of these variants in each population is believed to stem from the protective effects against Plasmodium Falciparum malaria [6].

G6PD variants associated with hemolysis destabilize the enzyme. Elucidation of the crystal structure of G6PD has revealed that disease associated mutations result in misfolding of the protein making it more susceptible to proteolytic degradation [7]. Because mature Red Blood Cells do not synthesize new proteins,G6PD A- or G6PD Mediterranean enzyme activity fall quickly, as red cells age, to the level inadequate to protect against oxidative stress. G6PD deficient red cells are more susceptible than normal cells to oxidative damage; the reason for this is that NADPH, produced by G6PD is required for the regeneration of Glutathione (GSH) which in turn detoxifies Hydrogen peroxide via GSH peroxide1. Oxidative damage can be caused by hypoxia, bacterial infection and a number of drugs. G6PD deficiency causes episodic [illegible]sis which seem to involve the following sequence. When G6PD deficient cells are exposed to a

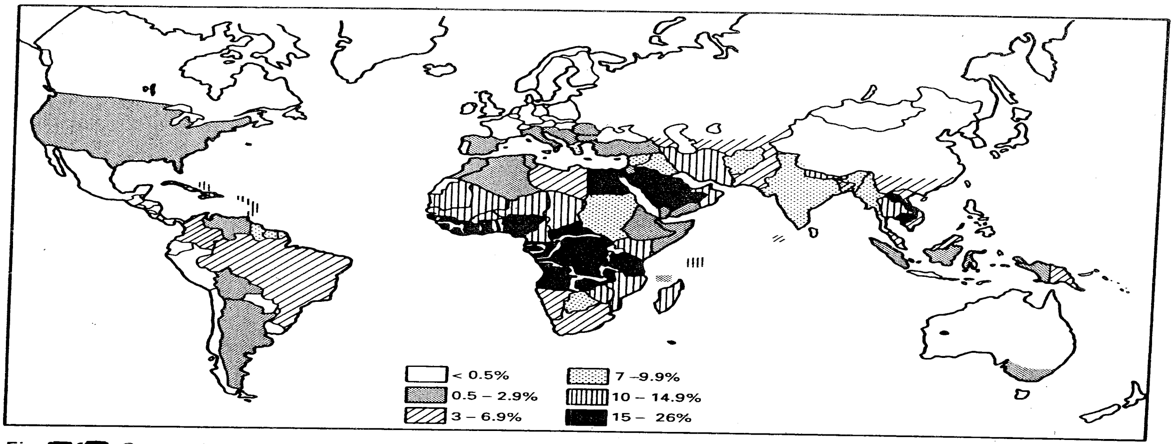

Fig. 1 Geographic distribution of G6PD deficiency (reproduced with permission of the World Health Organization, Geneva.)

Figure: Geographic distribution of G6PD deficiency (reproduced from World Health Organization)

high level of oxidatants, there is oxidation of reactive sulfhydral group as globin chains, which become denatured and form a membrane bound precipitate known as Heinz bodies [4]. These are seen within the Red Cells and are stained with Crystal Violet as dark inclusions. Heinz bodies can damage the membrane sufficiently to cause intravascular hemolysis.Less severe membrane damage result in decreased Red Cell deformability. As inclusion bearing cells pass through the splenic cords, macrophages pluck out Heinz bodies. Due to membrane damage, some of these partially devoured cells retain abnormal shape appearing to have a bite of cytoplasm removed, (bite) cells [4].Other less severely damaged cells revert to spherocytes and are highly prone to trapping in splenic cords and rapid removal by erythrophagocytosis. Our study shows relatively high frequency (4.5%) of G6PD deficiency as against (1.8%) in a local study [8]. The reasons may be due to the difference in sensitivity of the method used for detection of G6PD deficiency or variation of the ethnic population tested.

The severity of hemolysis varies from mild anemia and jaundice requiring only a few days bed rest to severe life threatening anemia requiring urgent blood transfusion. The acute attack can lead to massive hemoglobinuria and renal failure. G6PD is an important cause of neonatal jauindice. Rare individuals have G6PD mutation producing an enzyme variant which is so severely abnormal quantitavily, or so severely deficient quantitavely that they suffer a life long anemia.

It has been reported in recent litrature that clostridium defficile infection can precipitate severe hemolysis in G6PD deficient preterm infants [9], severe complications of lower respiratory tract infection can be seen in patients with G6PD deficiency and that G6PD deficiency also enhances human corona virus 229E infection [10]. Morphologically the anemia is normocytic and normochromic with Reticulocytosis. Diagnosis requires G6PD assay. Most patients are well adjusted to their anemia and usually require no treatment except Folic acid supplements. The bone marrow shows erythroid hyperplasia without evidence of ineffective erythropoesis so there is no indication for a chronic blood transfusion.

The diagnosis is generally suspected when a patient from certain ethnic group develop anemia, jaundice and symptoms of hemolysis. The confirmation is done by G6PD Screening and DNA test. For treatment, the most important measure is prevention, diagnosis of the deficiency while asymptomatic and avoidance of drugs and food that can trigger hemolysis.As a preventive measure US Army has mandated that all troops should be screened for G6PD deficiency before being deployed in the malarious regions [11].

In acute phase of hemolysis blood transfusion might be necessary or even dialysis in acute renal failure. Blood transfusion is an important symptomatic measure as the transfused red cells are generally not G6PD deficient. Some patients benefit from splenectomy. Folic acid should be used in any disorder featuring a high red cell turn over. Although Vit E and Selenium have antioxidant properties their use does not decrease the severity of G6PD induced hemolysis

CONCLUSION

G6PD deficiency is the most prevalent enzymopathy throughout the world. World Health Organization has mapped the frequency of the disease throughout the world and in Pakistani population the frequency, according to WHO, is 3-6.9%. Our study shows the frequency to be 4.5% which is in conformity with the W.H.O data.

REFERENCE

1. Geographical distribution of G6PD deficiency, WHO report. In:.Hoff Brand A V and Lewis S M Editors. Postgraduate Hematology 3rd ed C B S. 1991; p: 167-173.

2. Luzzatto L, Testa U (1987). Human erythrocyte glucose-6-phosohate dehydrogenase: structure and function in normal and mutant subjects. Current Topic in Haematology, 1. 1-70.

3. Capallini MD, Fiorelli G.Glucose 6 phosphate dehydrogenase deficiency. lancet 2008: 5; 371 (9606) 64-67

4. Aster C J .Red blood cells and bleeding disorders, In: Kumar V, Abbass A, and Fausto N Editors. Robbins & Cotran.Pathologic Basis of Disease; 7th ed. Elsvier 2004;p: 627-8

5. Mehta A, Mason PJ, Vulliamy TJ. Glucose-6-phosphate dehydrogenase deficiency. Bailliers Best Pract Res Clin Hematol 13:21, 2000.

6. Tishkoff SA. Haplotype diversity and linkage disequilibrium at human G6PD def: recent origin of alleles that confer malarial resistance. Science, 2001, 293: 455.

7. Gomez –Gallego F. Structural defects underlying protein dysfunction in human glucose-6-phosphate dehydrogenase A (-) deficiency J Biol Chem.2000: 275.

8. Anwar M, Ayyub M, Bhatti FA, Nadeem M, Nadeem A. Frequency of G6PD deficiency in some ethnic groups of Pakistan.J Coll Physicians Surg Pak.2005; 15: 3: 137-41.

9. Lodha . MS, Kelly E, Amin H.Clostridium defficile infection precipitating hemolysis in G6PD deficient preterm twins causing severe neonatal jaundice. J Perinatol 2008 Jan; 28: 77-8.

10. Wu YH ,Tseng CP,Cheng ML,Ho HY,Shih SR,Chiu DT.G6PD deficiency enhances corona virus 229 E infection. J infect Dis 2008 Mar 15; 197: 6; 812-6.

11. Murray, Clinton K,Chinevere, Tory D,Grant, Earl et al .Prevalence of G6PD deficiency in U.S Army Personnel. Jr. Mil Med 2006; 171: 9: 905-7

.....