FREQUENCY OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY AMONG THE ASYMPTOMATIC HEALTHY INDIVIDUALS

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ABSTRACT

Objective: To determine the frequency of G6PD deficiency among the asymptomatic healthy individuals.
Study Design: Cross sectional study.
Place and Duration of study: This study was done at Pakistan Air Force (PAF) Hospital Islamabad and PAF Hospital Lahore from July 2015 to March 2017.
Patients and Methods: The candidates tested were of both genders that came from all provinces of Pakistan for Central Medical Board selection in PAF or admission in PAF Public Colleges, Sargodha and Lower Topa. Their minimum age was 11 year and maximum 28 year. Their screening test for G6PD deficiency was carried out on Tuber by Merux Pty Ltd Australia. It is a qualitative, colorimetric procedure using dichlorophenol indophenols as an indicator for determining G6PD deficiency.
Results: A sum of 1289 subjects was enrolled in the study. Out of them 1150 (89.2%) were male and 139 (10.8%) were females. Among 1150 males, 21 (1.82%) were found deficient for G6PD whereas only 1 (0.7%) female was G6PD deficient. A frequency of 1.7% was found in all subjects. All the candidates had normal blood counts except for 33 females who were anaemic with hemoglobin levels < 12.0 g/dl.
Conclusion: In this study a frequency of 1.7% was found in all subjects. G6PD deficiency can present in apparently healthy individuals and remain undiagnosed even in third decade of life. G6PD screening can be included in normal health screening profile at least once in lifetime.
Keywords: Glucose-6-phosphate dehydrogenase, G6PD, NADPH, Haemolysis.

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INTRODUCTION

The red cell enzyme disorder due to Glucose-6-phosphate dehydrogenase (G6PD) deficiency was first revealed by Alving and his colleagues in 1956 [1]. They were investigating the unusual primaquin sensitivity of erythrocytes. The incidence of G6PD deficiency all over the world is highly variable. In Middle East and Central Africa, an incidence of 26% is reported in common population whereas it is less than 0.5 % in Scandinavian countries, North Europe, Russia, UK and Northern China. The incidence of G6PD deficiency in Pakistan varies from 3% to 6.9% [2-5].

The inheritance of G6PD deficiency is X-linked. The red blood cells are dependent for most of their metabolic energy on Embden-Meyerhof pathway. The function of hexose monophosphate shunt of the Embden-Meyerhof pathway is to provide NADPH to reduce oxidized glutathione through glutathione reductase. The deficiency of G6PD exposes the red blood cells to oxidative stress and ultimately haemolysis. G6PD deficient individuals are specifically exposed to haemolysis during infection or when exposed to certain drugs. The rationale of the study is to determine the frequency of G6PD deficiency among the asymptomatic healthy individuals.

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MATERIALS AND METHODS

This cross-sectional study was done at PAF Hospital Islamabad and PAF hospital Lahore from July 2015 to March 2017. The candidates tested were of both genders that came from all provinces of Pakistan for Central Medical Board selection in PAF or admission in PAF Public Colleges, Sargodha and Lower Topa. Their minimum age was 11 year and maximum 28 year; mean age was 20.2 ± 5.74 years. All candidates that were asymptomatic and found unremarkable on physical examination without signs of chronic hemolytic anemia were enrolled in this study. Candidates having reticulocyte count more than 3.0% were excluded from study. Their complete blood count was analyzed on Sysmex KX 32 automated hematology analyzer. Reticulocyte count

was calculated on brilliant cresyl blue stained slides. Their screening test for G6PD deficiency was carried out on Tuber by Merux Pty Ltd Australia. It is a qualitative, colorimetric procedure using dichlorophenol indophenols as an indicator for determining G6PD deficiency.

RESULTS

A sum of 1289 subjects was enrolled in the study. Out of them 1150 (89.2%) were males and 139 (10.8%) were females. Out of 1150 males, 21 (1.82%) were found deficient for G6PD whereas out of 139(10.8%) females only 1 (0.7%) was G6PD deficient. A frequency of 1.7% was found in all subjects. All the candidates had normal blood counts except for 33 females who were anaemic with hemoglobin levels < 12.0 g/dl. None of the G6PD deficient individual was found anaemic. Their other baseline radiological (chest X-ray) and laboratory investigations were also normal.

Table-1: Table showing comparison of our study with studies reporting frequency of G6PD deficiency from different areas of Pakistan.

S #	Sample size	Frequency	Reference
1.	888	4.5%	Mehmood et al.[20]
2.	277	3.97%	Younas et al.[3]
3.	3000	1.8%	Ali et al.[21]
4.	3600	1.36%	Khan et al.[4]
5.	1289	1.7%	Our study

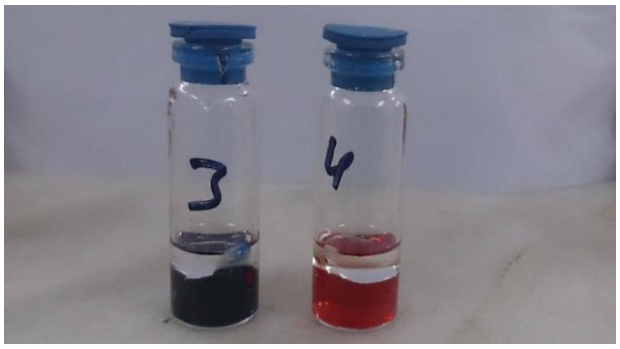

Figure-1: Showing a normal control on the right and a G6PD deficient sample of our study on the left.

DISCUSSION

One of the commonest enzymopathy of red blood cells in the world is G6PD deficiency [6]. Around the globe there are approximately 0.4 billion people suffering from this disease. The disease primarily affects males since it is an X-linked disorder. However, females can be clinically affected those who are carriers due to randomization of X-chromosome.

G6PD is the enzyme controlling flux through pentose phosphate pathway. It catalyses the initial phase of the pathway. The availability of NADP + is must for this activity. Two molecules of NADPH are produced in this pathway. The first NADPH is obtained when G6P is converted into 6PG. whereas; the second molecule is produced through oxidation of 6PG into ribose - 5 - phosphate. The red cell survival is dependent on availability of NADPH which in term promotes glutathione reduction. Unlike other cells, red blood cells lack mitochondria and are dependent on pentose phosphate pathway for NADPH. The G6PD deficiency and ultimately NADPH exposes the patient red cells to oxidative stress with accumulation of free radicals and ultimately haemolysis [7,8].

G6PD enzyme deficiency has different variants. Total number of variants described so far is at least 127. [9]. These variants can be classified into five different groups in relation to their activity to wild type G6PD. G6PD A^- variant is commonest in African population whereas the Mediterranean variant and G6PD Canton are frequent in population of Italy and southern China respectively [10-18].

G6PD deficiency is characterized by four clinical syndromes. The four syndromes are favism, neonatal jaundice, drug induced hemolytic anemia and chronic non spherocytic hemolytic anemia. In all four syndromes the triggering factors for haemolysis include: infection, drugs and oxidative food. Age is one of the modifiers for clinical effects. Clinical presentation of all syndromes differs. According to WHO classification of G6PD deficiency; it is divided into four classes. In Class I chronic non spherocytic haemolytic anaemia is included, in class II favism, class III includes drug induced haemolytic anaemias whereas, neonatal jaundice syndrome falls in all of above three classes variants [9,19].

G6PD enzyme assay is the diagnostic test for G6PD deficiency. False normal test can result due to reticulocytosis secondary to haemolysis as new red cells are well replenished with enzyme. Monospot flurorescent test, methaemoglobin reduction test, dye decolourization test and formazan test are among the screening tests employed for G6PD detection. G6PD enzyme assay for G6PD screening is also available in Pakistan. The screening of carriers is difficult through conventional detection methods as they can present with normal or close to normal G6PD enzyme activity. In our study dye decolourization test is used for screening of our candidates.

The overall frequency of deficiency in our study was 1.7%. This is quite comparable to other local studies and WHO report.

CONCLUSION

In this study a frequency of 1.7% was found in all subjects. G6PD deficiency can present in apparently healthy individuals and remain undiagnosed even in third decade of life. Moreover, it can also present with normal haemoglobin levels. G6PD screening can be included in normal health screening profile at least once in lifetime

AUTHORS CONTRIBUTION

Muhammad Arif Sadiq: Data collection, concept and manuscript writing

Ahmad Muqeem: Overall supervision and data analysis

Asma Bilal: Literature review and data tabulation

Rizwan Hashim: Data interpretation

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