FREQUENCY OF TOXOPLASMOSIS IN CHILDREN WITH GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY

Sawsan Issa Habeeb, Aida Abdulkareem, Ghalib Noori

ABSTRACT

A prospective study was carried out to evaluate the frequency of toxoplasmosis in children with glucose-6-phosphate dehydrogenase deficiency at Basrah General Hospital and Basrah Maternity and Children Hospital for 1 year (from October 2004 - October 2005). One hundred ten children (6 months - 60 months) of age were screened for both toxoplasmosis antibodies and glucose-6-phosphate dehydrogenase deficiency; fifty (45.5%) children had glucose-6-phosphate dehydrogenase deficiency, 48% of them had toxoplasmosis. The reminder sixty children (54.5%) had normal glucose-6-phosphate dehydrogenase activity; among them fifteen (25%) had toxoplasmosis. From this study it was concluded that acquired toxoplasmosis was significantly higher among children with G6PD deficiency compared to those of normal G6PD activity.

INTRODUCTION

Glucose-6-phosphate dehydrogenase deficiency (G6PD), the most common enzymatic deficiency worldwide, causes a spectrum of diseases including neonatal hyperbilirubinemia, acute hemolysis, and chronic hemolysis, this x-linked inherited disorder affects approximately 400 million people worldwide[1]. It is distributed in the Mediterranean region, across Middle East including Iraq[2], India, Indonesia, South China as well as Middle Africa, with an incidence over 1%[3]. The over all incidence of G6PD deficiency varies from 8%-50% in the Arab Word[4]. The frequency of G6PD deficiency 18% in Eastern Province of Saudi Arabia& 8.4% for the western province[5,6]. In Iraq (6.1%) were G6PD deficient[2]. In Basrah; southern Iraq, G6PD deficiency was detected in (12.5%) of people[7]. Patients with G6PD deficiency are predisposed to bacterial infections of variable severity. The underlying immune deficiency is due to phagocytic killing defect. An unusual propensity for infection with catalase positive organisms has been reported in patients with severe deficiency or complete absence of G6PD[4,8]. In normal person there are two host defense mechanisms, non-specific and specific types, the non-specific ones include physical and chemical barriers as well as complement system and phagocytic cells, the specific ones are the cell mediated immune responses, both mechanisms are involved in host defense against toxoplasma infection[9,10]. The parasite *Toxaplasma gondii* infects between 30-60% of people across the world. Most human infections are benign; in adults and children past the neonatal period, the disease is usually asymptomatic. Nevertheless, a generalized infection probably occurs. When symptoms are seen, they are most frequently mild and the disease picture simulates infectious mononucleosis. Diagnosis of toxoplasma infection is seldom made by recovery of the parasite; usually it is done by serological tests[11]. The prevalence of toxoplasmosis was (41.1%-52.1%) in a community–based sero-epdemiological study done in 3 areas (rural, urban and suburban semi rural) in Basrah governorate, southern Iraq[12]. In some variants of G6PD deficiency with absent leucocyte G6PD, there may be abnormal leucocyte function and such subjects present with infection similar to chronic granulomatous disease[9]. Literature reports have shown increase frequency of G6PD deficiency in the red cells of patients with typhoid fever as compared to general population[13,14] and increased susceptibility to catalase-positive bacterial infection in red cells among G6PD deficient newborn infants[15]. In addition, an increased increase incidence of specific infections such as viral hepatitis is also found in G6PD deficiency[4,6,16]. This study was carried out to assess the frequency of toxoplasma antibodies among children who had G6PD deficiency in comparison to children with normal G6PD activity.

PATIENTS AND METHODS

One hundred ten children (6-60) months of age were included in the study, all were presented with mild acute illnesses as upper respiratory

Sawsan Issa Habeeb, MBChB, FICMS, Department of Pediatrics, College of Medicine, University of Basrah.
Aida Abdulkareem, MBChB, CABP, Department of Pediatrics, College of Medicine, University of Basrah.
Ghalib Noori, Bacteriologist, General Public Health Lab.

tract infections or diarrhea, (children with chronic illnesses were excluded), those children were attending outpatient clinic in Basrah General Hospital and Basrah Maternity and Children Hospital for 1 year (from October 2004-October 2005). All children were normal on examination showing no abnormal physical signs. Malnourished children, children with chronic illnesses or those who had positive physical signs were not included in the study.

***Toxaplasma antibodies estimation*:-**

Four milliliters of blood was aspirated from each child, 2 ml were put in separate test tube, centrifuged and the serum was screened for toxoplasma serum titer by indirect fluorescence antibody test technique, the children with positive titer were considered to have acquired toxoplasma infection because all of them were more than six months of age.

G6PD estimation

Other 2 ml of blood were put in test tube with 0.4 ml of anticoagulant (sodium citrate and citric acid) then 0.1 ml of sodium nitrate and 0.1 ml of methylene blue were added to it, then was put in the incubator for 3 hours, after that change of the color was assessed as screening for G6PD deficiency, red color was regarded as normal G6PD activity, brown color was regarded as intermediate deficiency deep brown was regarded as full or severe deficiency[17]. Children were divided into two groups, those with normal G6PD activity and those with G6PD full deficiency. (Intermediate deficiency was not considered in our study). Toxoplasma serum titers were assessed in both groups and the frequency of positive toxoplasmosis was compared in G6PD deficient group with group of normal G6PD activity. For sake of statistical analysis Chi-square (x^2) test was used, the significance level was set as P<0 .05

RESULTS

One hundred ten children were included in the study; 50(45.5%) had severe G6PD deficiency while 60(54.5%) had G6PD normal activity. In G6PD deficient group, 24 (48%) had positive titer for toxoplasmosis, the remaining 26(52%) had negative toxoplama serum titer. (Table-1)

Among group of normal G6PD, 15(25%) had positive toxoplasma titer while 45(75%) were negative for toxoplama titer. The infection rate was 48% in G6PD deficiency group while it was 25% in G6PD normal group.

X^2=6.3, P-value < 0.025, so the results were statistically significant.

Table 1. ***Observed frequency of Toxoplasma positive titer in G6PD deficient versus G6PD normal children***

Toxoplasma titer	G6PD deficiency		G6PD normal		Total	
	No.	*%*	*No.*	*%*	*No.*	*%*
Positive	24	48	15	25	39	35.4
Negative	26	52	45	75	71	64.5
Total	50	45.5	60	54.5	110	100

Chi square=6.3,
P-value <0.05, the results were statistically significant

DISCUSSION

Toxoplasma gondii is ubiquitous intracellular protozoal parasite; the infective form can stimulate an inflammatory response and has capacity to invade the cells of reticuloendothelial system and neural cells, in immunologicaly normal children acute acquired infection may be asymptomatic, or causes lymphadenopathy[10]. While the effect of G6PD deficiency on red blood cells (RBC) is well known, there is less information available regarding the effect and impact of G6PD deficiency in polymorph nuclear neutrophils (PMNs) functions and its clinical impact[4].

In this study the rate of **toxoplasma** infection was compared in children with G6PD deficiency versus children of normal G6PD activity. It was found that toxoplasma infection was higher among G6PD deficient children, this result was similar to study done at Saudi Arabia at 1995[6]. The likely explanation is due to both direct destruction of the reticuloendothelial system by **toxoplasma** organisms and decreased killing of the phagocytic cells, this is clear from the fact that when polymorph neutrophils (PMNs) are stimulated, the enzymatic

nicotinamide adenine dinucleotide phosphate (NADP) oxidase system is activated resulting in the production of free oxygen radicals, which are essential for killing phagocytized microorganisms[18]. The impairment of this PMN metabolic process leads to inability of host defenses to kill ingested pathogen. This is well demonstrated in patients with chronic granulomatous disease (CGD) who suffer from recurrent infections[19]. As G6PD is also involved in the regeneration of NADP which is required for bactericidal activity of PMN, as expected that PMN G6PD deficient would affect their killing ability and be clinically associated with recurrent infections[19]. G6PD deficient leucocytes result in defective pentose monophosphate shunt and however G6PD deficient leukocyte can kill organisms which produce hydrogen monoxide and were catalase negative[9], so impaired bactericidal activity will result since the PMNs bactericidal activity is dependent on NADP production catalyzed by G6PD[1]. Although toxoplasmosis has been considered important opportunistic infections in immunosupressed patients but still its prevalence is high in Basrah among normal population[20]. The relatively high levels of infection with *Toxoplasma gondii* indicates intimate contact with cats and dogs[12].
This can explain the occurrence of toxoplasmosis in children with normal G6PD activity in 25% of them as demonstrated in (Table-1).

It was concluded that G6PD is regarded as risk factor for toxoplasmosis so it is recommend to do further study to assess bactericidal activity of PMNs in children with G6PD deficiency and to measure G6PD level in PMNs suspension not only in whole blood, and to assess toxoplasma antibody titer in children with G6PD deficiency even if they are asymptomatic as asymptomatic acquired toxoplasmosis might in fact represent a serious and highly underestimated public health problem as cysts which are formed in the nerves and muscle tissue could reduce people's ability to concentrate, so could cause central nervous system manifestations[11].

REFERENCES

1. Jennifer E, Frank. Diagnosis and management of G6PD deficiency. Am- Fam- phys.2005; 72(7), 1277-1281.
2. Hilmi FA, Al-Allawi NA. Red cell glucose-6-phosphate dehydrogenase phenotypes in Iraq. Eastern Mediterranean Health J. 2002; 8(1).
3. TK chan EYang KD. G6PD deficiency, a review htm 2003; (1-13).
4. Atif H. Asghar, Kasim O. Ardati. Bactericidal activity of PMNS in individual severely deficient in G6PD. Saudi Medical J. 1995; 16:102-104.
5. Esien A. Usanga[a]. Glucose-6-Phosphate Dehydrogenase Deficiency in Kuwait, Syria, Egypt, Iran, Jordan and Lebanon. International J. human &medical genetics. 2000; 50(3) 158-16.
6. Tabbara KF, Shrara NA. Toxoplasmosis In group of G6PD deficiency patients. Saudi Medical J. 2001; 22 (4).
7. Hassan MK, Taha JY. Frequency of haemoglobinopathies & glucose-6-phosphate dehydrogenase deficiency in Basra. Eastern Mediterranean Health J. 2003; 9.
8. Vives Corrons Jl, Feliu E. Severe G6PD deficiency associated with chronic hemolytic anemia, granulocyte dysfunction & increase susceptibility to infection; description of a new molecular variant. Blood disease J. 198; 59:432-434.
9. Copper MR, Dechatelet LR. Complement deficiency of leukocyte G6PD with defective bactericidal activity. J. clin. Invest. 1977; 51:769-778.
10. Mcleod R, Remington JS. Infectious diseases, toxoplasma gondii. Behraman, Kliegman. Nelson text book of Pediatrics. 17th edition 2004; 1054-1062.
11. Razzak AH, Wais SA. Toxoplasmosis: the innocent suspect of pregnancy wastage in Duhok, Iraq Eastern Mediterranean Health J. 2006; 12, 2005; 11.
12. Yacoub A.AH, Bakr S, Hameed AM. Seroepidemiology of selected zoonotic infections in Basra region of Iraq. Eastern Mediterranean Health J. 2006; 12(1,2).
13. Lampe RM, Kirdpon S. G6PD deficiency in children with typhoid fever in China .J.Pediatric.1975; 87:576-578.
14. Owusu SK, Foli AK. Frequency of G6PD deficiency in typhoid fever in China. Lancet 1972; 1:320.
15. Abu-osba YK, Mallouh AA. Incidence& causes of sepsis in G6PD deficiency in newborn infants'. J. Pediatric. 1989;114:748-752
16. Israel Gotman, Mordechai Muszkat .Glucose 6PD deficiency associated with increased initial clinical severity of acute viral hepatitis A. J. Gastro enterology& hematology. 2001; 16, 1239.
17. Mitchell Lewis S, John Dacie. Practical Haematology. G6PD Screening. 9th edition. Churchill Livingstone 2001, 435.
18. Yang KD, Hill HR. Neutrophil disorders, pathophysiology, prevention &therapy. J. Pediatric. 1991; 119: 343-354.
19. Forehand JR, Nauseef WM. Inherited disorders of phagocyte killing In: Scriver CR,Beaudet Al. The metabolic and molecular bases of inherited Dis 7th edition. 1995; 3995-4026.
20. Nadham KM, Maha M.Al-Mahfouz. Toxoplasmosis among Selected groups of children. Kufa Medical J. 2006. 9(2) 310-314.