Toxoplasmosis in a group of glucose-6-phosphate dehydrogenase deficient patients

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ABSTRACT

Objectives: This was a retrospective study that aimed at evaluating the relative risk of Toxoplasma infection in patients with glucose-6-phosphate dehydrogenase deficiency as compared to a control group with no glucose-6-phosphate dehydrogenase deficiency.

Methods: Ninety-one blood donor volunteers had serology testing from *Toxoplasma gondii* and were screened for glucose-6-phosphate dehydrogenase deficiency by a qualitative method using fluorescent spot test. They were all males and their ages ranged from 17 to 52 years.

Results: Fifty-three persons (58%) were glucose-6-phosphate dehydrogenase deficient and 38 (42%) were glucose-6-phosphate dehydrogenase normal. In the glucose-6-phosphate dehydrogenase deficient group, 31 (58.5%) had positive titers for Toxoplasma; while in the glucose-6-phosphate dehydrogenase normal group 9 persons (24%) had positive titers for Toxoplasma. The relative risk of infection was 2.5 times more in the glucose-6-phosphate dehydrogenase deficient group, a statistically significant difference with a p value of 0.002.

Conclusion: Glucose-6-phosphate dehydrogenase deficiency seems to increase the risk for Toxoplasma infection by 2.5 fold probably due to decreased killing effect, of phagocytic cells.

Keywords: Glucose-6-phosphate dehydrogenase deficiency, neutrophils respiratory burst, pentose monophosphate shunt, *toxoplasma gondii*.

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Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common genetic abnormality among Saudi Arabs. The incidence of G6PD deficiency varies from one region to another in the Kingdom. The overall incidence of G6PD deficiency is 18% in the eastern province.[1] Both African and Caucasian variants are present.[2] Patients with G6PD deficiency are predisposed to bacterial infections of variable severity. The underlying immunodeficiency is due to phagocytes killing defect. An unusual propensity for infection with catalase-positive organisms has been reported in patients with severe deficiency or complete absence of G6PD.[3] There are 2 host defense mechanisms, of 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 and antibody-mediated immune responses. Both mechanisms are involved in host defense against Toxoplasma infection. The aim of this study was to compare the rate of Toxoplasma infection in a group of Saudi patients with G6PD deficiency with a group of normal controls.

Methods. Ninety-one blood donor volunteers were screened at the Blood Bank in King Saud University Hospital for Toxoplasma serum titers by Abott enzyme-linked immunosorbent (ELISA) technique. They were screened at the same time for

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Table 1 - Observed frequency of Toxoplasma positive titers in G6PD deficient versus G6PD normal blood donor volunteers.

Toxoplasma Titer	G6PD Deficient (%)	G6PD Normal (%)	Total (%)
Positive	31 (58.5)	9 (24)	40 (44)
Negative	22 (41.5)	29 (76)	51 (56)
Total	**53 (58.0)**	**38 (42)**	**91 (100)**
Relative risk = 58.5/23.7 = 2.47 (approx 2.5X) Yates chi square p value 0.002 G6PD - Glucose-6-phosphate dehdrogenase			

G6PD deficiency by a qualitative method using fluorescent spot test. They were all males and their ages ranged from 17 to 52 years.

Results. Table 1 shows the observed frequency of positive Toxoplasma serum test in volunteers with G6PD deficiency versus those with normal G6PD level. Of the 91 persons, 53 (58%) were G6PD deficient and 38 (42%) were G6PD normal. In the G6PD deficient group, 31 persons had positive titers for Toxoplasma with IgG levels ranging from 16.4 IU/ml to 266.3 IU/ml. One person had positive IgM titer and IgG was negative. The remaining 22 had negative Toxoplasma serum test. That constituted a 58.5% infection rate among the G6PD deficient group (Table 1). Among the G6PD normal group, 9 had positive Toxoplasma titers and 29 were negative. The positive titers ranged from 9.4 IU/ml to 112.5 IU/ml. The infection rate among this group was 24%. The calculated relative risk of infection was found to be 2.5 times higher in the G6PD deficient group, a statistically significant difference with a p value of 0.002.

Discussion. *Toxoplasma gondii* is a ubiquitous intracellular protozoal parasite. The infective form (tachyzoite) can stimulate an inflammatory response and has the capacity to invade the cells of the reticuloendothelial system and neural cells. In the retina, the organisms proliferate within a cell to form a cyst and at this stage they become metabolically depressed and dormant bradyzoites. The pathogenic mechanism of cell invasion and destruction awaits clarification. Host defense mechanisms involve ingestion and killing of bacteria and other microorganisms by phagocytic cells (polymorphonuclear (PMN) cells, monocytes and non-motile phagocytic cells of the reticuloendothelial system). Degranulation of these cells leads to the release of proteases, cytokines and cationic proteins. Neutrophils contain the most powerful antibacterial agents including the newly described low molecular weight peptides, defensins (Table 2). However, cells and tissue damage is mediated mainly by free radicals released during the respiratory burst of neutrophils. Phagocytosis activates an oxidase that transfers an electron to oxygen which forms a superoxide anion, an unstable free radical.[4] The pyridine nucleotide nicotinamide adenine dinucleotide phosphate (NADPH) is the source of these electrons and hydrogen ions for phagocytic vacuoles (Figure 1). Two superoxide radicals can spontaneously form hydrogen peroxide (H_2O_2). Interaction between H_2O_2 and oxygen (O_2) forms hydroxyl free radicals (OH), a potent oxidizing agent. Myeloperoxidase catalyzes reactions between an oxidized halide such as chloride, iodide and hydrogen peroxide to form singlet oxygen.[5] Bacterial killing in normal phagocytes is inhibited by superoxide dismutase and catalase.[6] Glucose-6-phosphate dehydrogenase deficiency in leukocytes results in a defective pentose monophosphate shunt and reduced production of NADPH.[7] However, G6PD deficient leukocytes can kill organisms which produce hydrogen peroxide and were catalase negative.[8] This study showed an increased risk of Toxoplasma positive titers suggestive of sub clinical

Table 2 - Neutrophil antibacterial substances.

Category	Substance
Free radicals	Hydrogen peroxide
	Hypochlorite
	OH radical
	Nitric oxide
	chloramine
Enzymes	Proteinase 3
	Collagenase
	Elastase
	Cathepsin G
	Lysozyme
	Myeloperoxidase
	Azurocidin
	B-Glucoronidase
Peptides	Defensin
	B-Lysin
	Vasoactive intestinal peptides
Ion binders	Lactoferrin

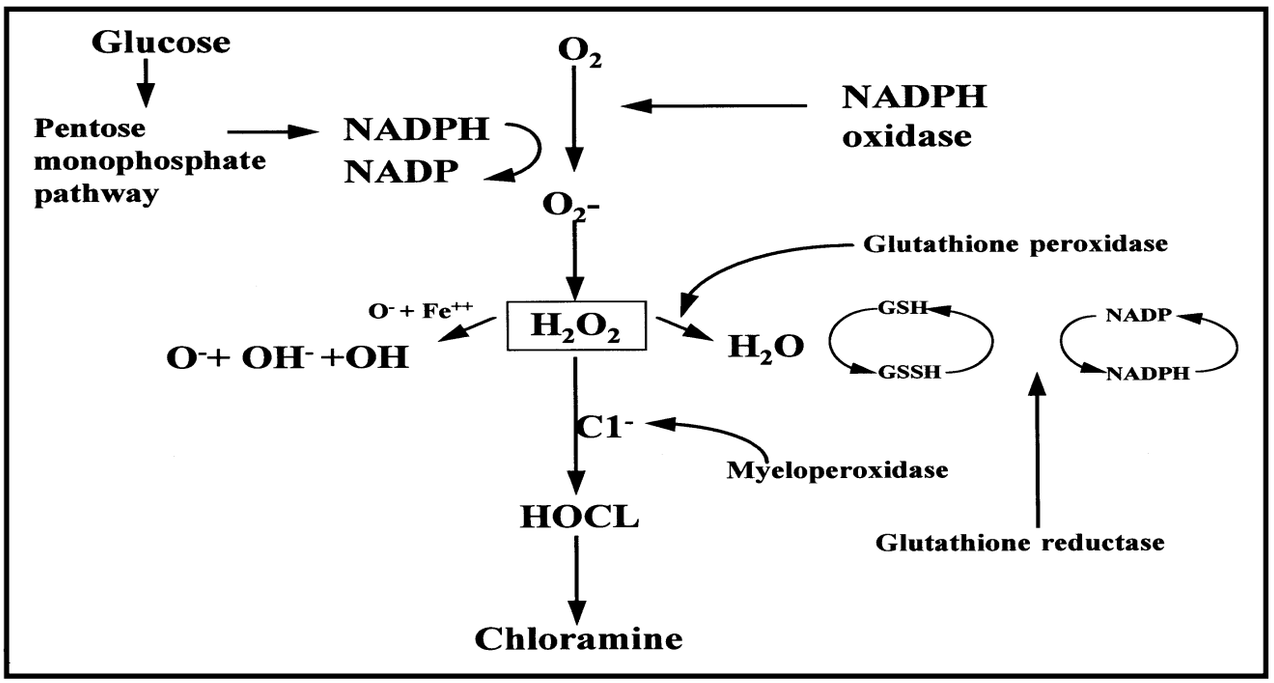

Figure 1 - The neurtrophil respiratory burst. Hydrogen peroxide is the central component and its metabolism which is dependent on the level of reduced glutathion, leads to further tissue damage.

infection by 2.5 folds in persons with G6PD deficiency as compared to G6PD normal individuals. This is in keeping with other findings of increased incidence of specific infections in populations with G6PD deficiency such as viral hepatitis and typhoid fever.[9-10] The likely explanation for the increased infection rate is due to both direct destruction of the reticuloendothelial system by Toxoplasma organisms and decreased killing effect of the phagocytic cells.

References

1. Abu-Osba YK, Mallouh AA, Hann RW. Incidence and causes of sepsis in Glucose-6-phosphate dehydrogenase deficient newborn infants. J Pediatr 1989; 114: 748-752.
2. Samuel AP, Saha N. Distribution of red cell G6PD and 6PGD phenotypes in Saudi Arabia. Trop Geogr Med 1986; 38: 287-291.
3. Vives Corrons JL, Feliu E, Pudjades MA, Cardellach F, Rozman C, Carreras A et al. Severe G6PD deficiency associated with chronic hemolytic anemia, granulocyte dysfunction and increased susceptibility to infection: description of a new molecular variant (G6PD Barcelona). Blood 1982; 59: 482-434.
4. Klebanoff SJ. Antimicrobial mechanisms in neutrophil polymorphonuclear leukocytes. Semin Hematol 1975; 12: 117-142.
5. Quie PG, Mill EL, Homes B. Molecular events during phagocytosis by human neutrophils. In: Brown EB, editor. Progress in Hematology. New York: Grune & Statton; 1977.
6. Allen RC, Stjernholm RL, Steele RH. Evidence for generation of an electronic excitation state(s) in human polymorphonuclear leukocytes and the participation in bactericidal activity. Biochem Biophys Res Commun 1972; 47: 679-684.
7. Babior M. Oxygen-dependent microbial killing phagocytes. N Engl J Med 1978; 298: 659-668.
8. Cooper MR, Dechatelet LR, McCall CE, La Via MF, Spurr CL, Baehner RL. Complete deficiency of leukocyte G6PD with defective bactericidal activity. J Clin Invest 1972; 51: 769-778.
9. Morrow RH, Smetana HF, Sai FT, Edgecomb JH. Unusual features of viral hepatitis in Accra, Ghana. Ann Intern Med 1968; 68: 1250-1264.
10. Lampe RM, Kirdpon S, Mansuwan F, Benenson MW. Glucose 6 phosphate dehydrogenase deficiency in Thai children with typhoid fevers. J Pediatr 1975; 87: 576-578.