

COMMON G6PD VARIANT FROM SAUDI POPULATION AND ITS PREVALENCE

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Biochemical characterization of erythrocyte glucose-6-phosphate-dehydrogenase from 18 unrelated deficient Saudi subjects from Al-Hassa and Al-Qatif areas of the Eastern Province was carried out according to WHO procedures. This has led to the identification of one genetically determined common variant, "G6PD Mediterranean." The overall prevalence rate of this deficiency in these areas was determined to be in excess of 42%. None of the subjects studied displayed any sign of favism, a condition usually associated with G6PD Mediterranean, which is characterized by a very low intracellular enzyme activity. *Ann Saudi Med* 1996;16(6):654-656.

The red blood cells (RBCs) contain glucose-6-phosphate-dehydrogenase (G6PD), designated according to its electrophoretic mobility as G6PD B(+). In Africa, a variant form, G6PD A(+) occurs, which has normal activity, but more rapid electrophoretic mobility than G6PD B¹. Human G6PD is encoded by an X-linked gene, the locus of which is polymorphic in several human populations.² Biochemical studies of variant phenotypes have led to the belief that polymorphism in different populations is often due to the occurrence of different genetically determined G6PD variants. Common inherited variants at the G6PD locus are mostly associated with an abnormally low level of enzyme activity.³ The enzyme deficiency is clinically relevant, since it is often associated with the risk of an acute hemolytic episode triggered by a variety of oxidant agents.⁴

This paper reports the biochemical characterization of G6PD variants commonly occurring in the Saudi population and their prevalence in the Al-Qatif and Al-Hassa areas. These two areas remain traditionally conservative communities, with relatively little admixture from outside populations.

Material and Methods

Over a period of two years, a total of 757 apparently healthy Saudi male volunteers, ranging from 20-45 years, were randomly selected from the Al-Qatif and Al-Hassa

oases in the Eastern Province of Saudi Arabia. Information was sought concerning the subjects' history of anemia, jaundice, blood transfusion, and the consumption of fava beans. Samples of whole blood were collected in heparinized tubes and were immediately transported in a refrigerated state to the laboratory. Hematological indices were determined for samples, using a hematology analyzer (Cell Dyn 700: Sequoia Turna, USA). Erythrocytes were placed in an ice bath and washed three times with cold PBS. Red blood cell G6PD activity levels and electrophoretic phenotypes were determined according to Battistuzzi et al.³ and Betke et al.⁵ Partial purification and biochemical characterization of the G6PD enzyme protein were performed as previously described.^{5,6}

Results

None of the subjects included in this study showed a history of anemia or jaundice following ingestion of fava beans, even though fava beans had been consumed regularly since early childhood. Prevalence rates of 45.9% and 36.5% for G6PD deficiency were found among the Saudi population of Al-Qatif and Al-Hassa respectively (Table 1). All subjects tested had a very low enzymatic activity and B-like electrophoretic mobility.

In order to carry out a complete biochemical characterization, the erythrocyte G6PD was partially purified from 18 randomly selected subjects from each area. The properties are summarized together with that of the "normal" control G6PD B (Table 2). The deficient enzymes show properties similar to those reported for G6PD Mediterranean. DNA from six deficient samples and nine control samples were also isolated and sent for molecular analysis. The analysis proved the presence of the common mutations found in the G6PD Mediterranean

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variant, characterized by a single C-T transition at nucleotide position 563, causing a serine phenylalanine replacement at amino acid position 188.⁷

Discussion

Frequencies of G6PD deficiency in Saudis of the Eastern Province have been reported to be higher than in most other human populations.⁸⁻¹¹ Our estimated frequencies of 45.9% and 36.5% for the two major areas of the Eastern Province differ slightly from those reported by Gelpi.⁸ This may be due to the restricted locality chosen by the investigator. Moreover, these prevalence rates are found to be much higher than those reported in other parts of Saudi Arabia, which range from less than 5% in the central area to 24% in Khaiber (North West Province).^{9,11} The common G6PD-deficient variant found in most parts of the Middle East is the Mediterranean variant. Based on the finding of low enzymatic activity and B-like electrophoretic mobility, it is assumed that the common type found in Saudi Arabia is the G6PD Mediterranean variant.⁹ However, it is now clear that G6PD variant, indistinguishable by criteria (i.e., enzymatic activity and electrophoretic mobility), may in fact be heterogeneous.¹² Consequently, the full biochemical characterization according to the WHO procedures should be carried out. Our studies have shown that the vast majority of samples from the Eastern Province are of Mediterranean phenotype. The above conclusion is further confirmed by the molecular analysis of the G6PD gene

from another sample group in these areas.⁷

Although favism is usually associated with the Mediterranean variant of this enzyme,¹³ none of the subjects studied have experienced this condition. However, this observation has to be further investigated, since it is known that favism is much more common in children than adults. Moreover, the amount of fava beans consumed and the season in relation to harvesting bear a direct relation to the incidence of favism. In addition, those who are sensitive show striking variability from one exposure to the next, for reasons which are as yet unclear.¹⁴ The two areas studied are also known to be the major loci for sickle hemoglobin and the thalassemia genes.⁹ This increases the possibility of association of G6PD deficiency and these conditions among the populations. Our recent study of the interaction of sickle cell hemoglobin with G6PD deficiency did not show any ameliorating effect.¹⁵ However, a possible interaction with thalassemia may be responsible for the mild behavior of sickle cell anemia in this area. Moreover, a further in-depth investigation of possible interactions of hemoglobinopathies with favism is required.

The need for utilizing screening measures for early detection of the genetic defect is immediately apparent, once consideration is taken of the high probability of association of G6PD deficiency with other hemoglobinopathies, such as sickle cell anemia, which may lead to a more serious condition. In addition, there is a compelling need for introducing measures such as genetic counseling and public health education as part of the overall health and welfare services in the area.

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TABLE 1. Prevalence of G6PD deficiency in the Eastern Province of Saudi Arabia.

Subject	Area		Total
	Al-Qatif	Al-Hassa	
Deficient	140	166	306
Normal	165	286	451
Total	305	452	757
% Deficiency	45.9	36.5	42.7

TABLE 2. Comparison of the biochemical characteristics of G6PD variant found in the Eastern Province.

Subject	N	Activity*			Substrate analogue utilization**				Thermo- ⁺ stability	pH
		mU	%	EM	Km G6PD (μM)	Km NADP (μM)	dGP6D (% of G6P)	dNADP (% of NADP)		
Deficient	18	3	0-3	100	10.5±3.1	1.1±0.3	52.2±4.1	307±20	L	Biphasic peak at pH 6.5-10.5
Normal G6PD B	8	105±15	100	100	52±7	3.3±0.9	6.1±0.3	55±2	N	N

N=number of subjects; *enzyme activity is expressed as mU/10⁹ erythrocyte and as percentage of normal; Km=Michaelis-Menten term; EM=electrophoretic mobility as percentage of normal G6PD B; **expressed as percentage of natural G6P & NADP substrates; thermostability is N for normal, L for labile.

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