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Newborn screening for Glucose-6-Phosphate Dehydrogenase Deficiency in Eastern Province, Saudi Arabia.

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Abstract

Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is an x-linked recessive disorder expressed mostly in males. Patients with G6PD deficiency may present clinically with evidence of hemolytic anemia in the neonatal period or later in life, or may remain asymptomatic. The aim of this study was to determine the incidence of G6PD deficiency in Saudi infants screened at birth. All Saudi infants born at Saad Specialist Hospital in Al-Khobar, Saudi Arabia between January 2005 and January 2006 were screened for G6PD at birth. Umbilical cord blood samples were taken and analyzed using ultraviolet quantitative kinetic method. Results showed that out of 1366 infants screened at birth G6PD deficiency was confirmed in 173 infants (incidence 126 per1000 live birth). One third of the G6PD-deficient infants were females. More than half of G6PD-deficient infants had severe enzyme deficiency while 37 (21.3%) developed neonatal jaundice requiring phototherapy. In conclusion the incidence of G6PD deficiency was high in the screened infants.

Keywords: Glucose-6-phosphate dehydrogenase deficiency, screening, newborn

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Introduction

Glucose-6-phosphate dehydrogenase deficiency (G6PD) is an X-linked inherited disorder most commonly affects people of African, Asian, and Middle-Eastern origin [1-8]. G6PD deficiency is one of the commonest enzyme deficiencies in humans [1, 2, 9, 10]. Homozygotes and heterozygotes can be symptomatic, although the disease typically is more severe in persons who are homozygous for the deficiency [11, 12, 13]. G6PD catalyzes the first step in the pentose monophosphate pathway, to produce nicotinamide adenine dinucleotide phosphate hydroxide (NADPH) [3, 10]. NADPH protects cells from oxidative damage. Precipitants of cellular damage include; infection, drugs, and ingestion of fava beans [1, 2]. Red blood cells are at greater risk of damage as these cells lack the cellular organelles such as mitochondria that produce NADPH [2, 3,11]. Oxidant damage of hemoglobin leads to the precipitation of hemoglobin, which may be morphologically recognized as Heinz bodies [2].

The G6PD gene is located on the long arm of the X chromosome [2]. The advances in molecular biology explored the genetics of G6PD deficiency with hundreds of mutations reported [1-4, 10, 14, 15]. Different mutations cause different levels of enzyme deficiency, with various clinical manifestations. [1-3, 9, 10]. Some patients with G6PD deficiency present with neonatal jaundice or rarely chronic hemolytic anemia. Kernicterus has been reported in some patient with severe hemolysis [2].

The diagnostic test for G6PD is usually done by fluorescent spot test and based on the conversion of nicotinamide adenine dinucleotide phosphate to its reduced form in erythrocytes [2, 3, 13, 16, 17]. This test is also used for newborn screening for G6PD deficiency. False positive results are possible especially if the test is done during or shortly after acute hemolysis as young red cells have higher enzyme activity [2, 17]. Newborn screening identifies affected infants before the development of clinical signs which will help to reduce morbidity associated with this condition [3, 7, 18, 19]. The aim of this study was to determine the incidence of G6PD deficiency in Saudi infants screened at birth.

Material and Methods

All Saudi infants born between January 2005 and January 2006 at Saad Specialist Hospital (SSH) in Al-Khobar, Saudi Arabia, were screened for G6PD at birth. Umbili-

cal cord blood samples were taken and enzyme activity was determined by measuring the rate of absorbance change at 340 nm, due to the reduction of NADP to NADPH when a sample was incubated with Glucose 6 phosphate [2]. Glucose-6- phosphate dehydrogenase activity was calculated in relation to erythrocyte count. Commercially available kits (Cat. No.038 T, United Diagnostics Industry Dammam, Kingdom of Saudi Arabia) were used. Results were interpreted as the percentage of normal G6PD activity. Enzyme activity less than 10% of the lower limit of normal activity was classified as a severe deficiency, whereas the activity between 10 and 60% was classified as mild to moderate deficiency [2]. Reference range according to manufacturer was 120-240 mU/RBC in million.

Results

All infants born at our institute were screened for G6PD deficiency. G6PD was confirmed in 173(12.6%) infants out of 1366 Saudi infants born between January 2005 and January 2006. Table 1 show that 60% of G6PD-deficient infants had severe enzyme deficiency. One third of the G6PD-deficient infants were females. Table 2 shows that more than half of G6PD deficient females had severe enzyme deficiency. Thirty seven (21.3%) of G6PD-deficient infants developed neonatal jaundice requiring phototherapy (Table 2).

Table 1. *Characteristics of patients with G6PD deficiency*

Variable	Value	%
Sex		
Male	116	67.05
Female	57	32.95
Family history		
No	142	82.08
Yes	31	17.92
Birth weight		
<2.5 kgs.	16	9.25
> 2.5 kgs.	157	90.75
Gestational age		
<37 wks	19	10.98
>38 wks	154	89.02
Phototherapy		
No	27	
Single	31	
Double	5	
Triple	1	

Table 2. *G6PD severity and sex distribution in affected infants*

	Severe	Moderate
Sex		
Male	74	42
Female	30	27
Jaundice		
No	71	38
Yes	33	31

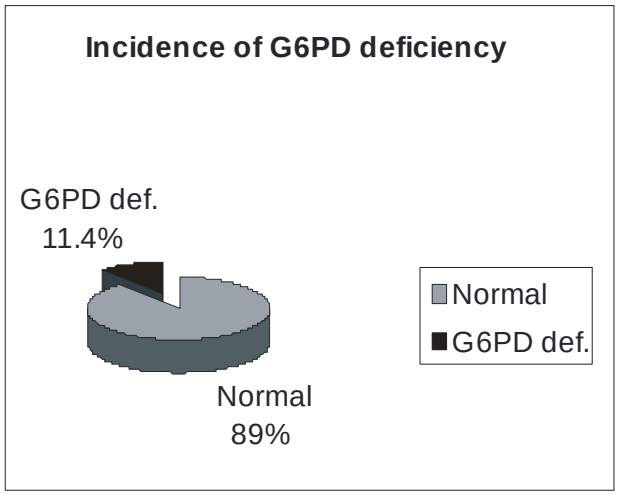

Figure 1. *Incidence of G6PD in 1366 infants screened at birth*

Discussion

Glucose-6-phosphate dehydrogenase deficiency, the most common enzyme deficiency worldwide, causes a spectrum of clinical features including neonatal hyperbilirubinemia, acute hemolysis, and chronic hemolysis. Persons with this condition may also be asymptomatic. G6PD occurs with increased frequency throughout Africa, Asia and the Middle East [1, 2, 4, 6-8,20- 24]. Most of the pathology associated with G6PD deficiency is preventable by early detection through universal newborn screening in areas where the disease is widely spread coupled with avoidance of precipitants of acute hemolysis. In this study the incidence of G6PD deficiency was high (126 per 1000 newborn infants) compared with other areas in Saudi Arabia [6, 7, 9, 16]. Muzaffer MA conducted a study on newborn screening for G6PD deficiency in the western province of Saudi Arabia and reported an incidence of 2% [7]. This difference in the incidence of G6PD deficiency between the eastern and western region of Saudi Arabia could be explained by the different tribes inhabiting this area and their different gene frequency of enzyme deficiency. In a study conducted in Oman about 27% of Omani males had inherited

glucose-6-phosphate dehydrogenase deficiency compared with 11% of females [8]. The high incidence of G6PD deficiency in the Middle East including our study population may be explained by the genetic makeup of this population in addition to the high incidence of consanguinity [20]. The World Health Organization recommends screening all newborns in populations with a prevalence of 3 to 5 percent or more in males [1]. Early detection of G6PD deficiency is important to avoid acute hemolysis that is caused by exposure to an oxidative stressor in the form of an infection, oxidative drug or fava beans.

It was reported that female heterozygote may be hard to diagnose because of X-chromosome mosaicism leading to a partial deficiency that will not be detected reliably by screening tests [3, 4]. In this study One third of the G6PD-deficient infants were females. This could be explained by the homozygosity of the mutated gene. As an x-linked disease, G6PD occurs in females when both parents are either affected or carrier of the disease. This agrees with the molecular genetic findings reported by Al-Ali et al who studied DNA of patients with G6PD deficiency in the eastern province of Saudi Arabia and found that the G6PD Mediterranean mutation is the most common in the Eastern Province, followed by G6PD A- [4]. The high incidence of G6PD deficiency in females in this study reflects the high incidence of G6PD deficiency in this community at large.

The main treatment strategy for G6PD deficiency is avoidance of oxidative precipitants such as drugs known to cause hemolysis, infection, and surgery [3, 15, 18, 19]. Neonatal hyperbilirubinernia may require treatment with phototherapy if serum bilirubin is moderately elevated, however exchange transfusion is indicated to prevent kernicterus when unconjugated hyperbilirubinemia is significantly elevated [2, 18]. One fifth of the G6PD-deficient infants in this study developed neonatal jaundice requiring phototherapy. Similar results were reported in previous studies [1, 2, 4, 6-9, 25, 26, 27]. Al-Abdi et al reported that two thirds of newborn infants who have G6PD deficiency and jaundice required phototherapy treatment [9]. Some patients with G6PD deficiency develop mild jaundice that persists for longer period. In this study no patient was observed with evidence of chronic hemolysis. This may be explained by the fact that the variant causes chronic hemolysis is generally uncommon and may be because it is related to sporadic gene mutation rather than the more common inherited gene mutation which is probably the case in the study population [1]. None of the G6PD deficient patients identified in this study needed exchange transfusion to treat hyperbilirubinemia. This could be explained by the fact that the result of screening is usually available in the beginning of the course of jaundice which alerts physician to initiate phototherapy early and accordingly to avoid exchange transfusion.

The limitations of this study include, infants screened were born in a single center and the study population is not large enough to draw a firm conclusion regarding the incidence in the community. However, this study gives an indication that G6PD represents a health problem in the Eastern Province of Saudi Arabia and provides evidence for feasibility and justification for universal newborn screening in this area.

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