

## CLINICAL PRESENTATION OF GLUCOSE-6- PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY: A PILOT STUDY

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### ABSTRACT

Sixty-six children with G6PD deficiency were evaluated retrospectively to ascertain the clinical features, etiology, ultimate outcome and population at risk. The occurrence of jaundice in 18 neonates (group I) was, contrary to other countries, in the form of neonatal jaundice type II. Sepsis, prematurity, hypoxia and acidosis were associating factors. 77.8% of neonates had exchange blood transfusions and 22% had kernicterus.

The occurrence of acute hemolytic anemia in 48 children (group II) was seen at  $3.4 \pm 1.6$  years of age and the factor initiating hemolysis in the majority of cases was fava bean ingestion. 79% of group II had at least one blood transfusion for severe anemia. Chronic anemia in 6.2% suggested congenital nonspherocytic hemolytic anemia.

Most patients had blood group O, thus showing a higher prevalence than the general population. Among children, the birth places in 22 cases were in the north (77.2%), the west (18.1%), and other parts (9.7%) of Iran. 30.4% of children had other family members with G6PD deficiency.

According to WHO and considering the prevalence of the disease in our country, lab screening tests are strongly recommended in the following situations: neonates with jaundice, males having blood group O, a family history of the disease and children from the north and west of Iran.

**Keywords:** Hemolytic anemia, Favism, G6PD deficiency.

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### INTRODUCTION

G6PD deficiency is the most common congenital shunt defect of red blood cells reported from different parts of the world.<sup>1</sup> In Iran, 10-14.9% of the male population is hemizygous for G6PD deficiency.<sup>2</sup> Different clinical presentations of the disease in the form of acute hemolytic anemia (AHA), neonatal jaundice (NNJ) and congenital

nonspherocytic hemolytic anemia (CNSHA) have been reported. NNJ may develop in some neonates but not in all G6PD deficient babies.<sup>6</sup>

The susceptibility to hemolysis in certain families or populations illustrates the interplay of hereditary and environmental factors in the development of the disease, which may become severe and lead to kernicterus, death or spastic cerebral palsy.<sup>2,6</sup>

## G6PD Deficiency

Regarding racial, environmental and cultural factors affecting hemolysis,<sup>4</sup> this study aims to clarify the various clinical presentations of the disease, initiating factors and ultimate outcome, and define the population at risk.

### PATIENTS AND METHODS

The medical records of children with G6PD deficiency were reviewed retrospectively from 1991 through 1995 at university-affiliated hospitals. G6PD activity was measured by G6PD fluorescent spot test and ascorbate cyanide test. Age, sex, onset of jaundice, other clinical manifestations, predisposing factors, and hemoglobin and bilirubin levels were reviewed. The data were analyzed to evaluate the role of enzyme deficiency in producing the different clinical patterns of the disease.

### RESULTS

Patients with G6PD deficiency (66) were divided into two groups. Group I, being comprised of 18 neonates, and group II, consisting of 48 children.

In group I, 4 (22.2%) were female, 14 (77.7%) had exchange blood transfusion, and sepsis was the incriminating factor in the majority of cases (Table I). The onset on NNJ was  $2.8 \pm 1.3$  days.

In group II, 15 (31.2%) were female. 11 (22.9%) had previous jaundice of whom 4 (8%) had hospital admissions and only 2 (4%) had exchange blood transfusions.

Jaundice and anemia occurred at  $3.4 \pm 1.6$  years of age. Fava bean ingestion was the initiative factor for hemolysis in the majority of cases (Table II).

14 children (29.1%) had a positive family history for G6PD deficiency and 3 cases (6.2%) had CNSHA.

Among children, the birth places in 22 cases were northern Iran (77.2%), western Iran (18.1%), and other parts of the country (9.7%) while the parents of others had migrated to the capital. Most of the patients had blood group O (Table III).

38 children (79.1%) had blood transfusions because of low hemoglobin levels. The mortality figure of 1.5% in this study was due to the inclusion of a comatose child.

### DISCUSSION

G6PD deficiency, an abnormality of the hexose monophosphate shunt, is the most common congenital enzymopathy of red blood cells,<sup>9</sup> affecting 130 million people worldwide (Fig. 1).<sup>7</sup>

Upon exposure to an offending agent, hemoglobin tends to precipitate in these patients, ensuing in hemolysis. The

Table I. Conditions accompanied with G6PD deficiency in group I.

Predisposing factor	No.	%
Sepsis	8	44.4
Prematurity	3	16.6
Hypoxia and acidosis	2	11.11
Maternal cotrimoxazole		
Consumption	1	5.5
Other	4	22.2
Total	18	100

Table II. Factors responsible for jaundice in group II.

Initiating factor	No.	%
Fava beans	24	50
Fava beans+URI	14	29.1
+ Oxidative	6	12.6
+ Viral hepatitis	2	4
URI	1	2
Insecticides	1	2
Total	48	100

Table III. The group distribution and lab findings in G6PD deficient patients.

Blood group	Neonates (%)	Children %
O	9 (50)	24 50
A	5 (27.77)	11 22.9
B	3 (16.66)	5 10.4
AB	0 (0)	2 4.1
Unknown	1 (5.5)	6 12.5
Hb (g/dL) (Mean±SD)	13.53±2.75	6.6±1.6
Bilirubin (mg/dL)	28.2±20.35	5.69±4.03

most obvious clinical presentation of G6PD deficiency is AHA and the prototype of it is favism.<sup>6</sup>

Fava bean ingestion initiated hemolysis in the majority of our cases. Although a possible role of viral infection in producing hemolysis has been reported,<sup>13</sup> only one of our children had clinically apparent viral infection.

Another syndrome of great clinical and public health importance is NNJ, which may develop in some neonates with G6PD deficiency. It is likely that there are two types of NNJ; type I, the common variant, which occurs as an exaggerated physiologic jaundice and may result from G6PD

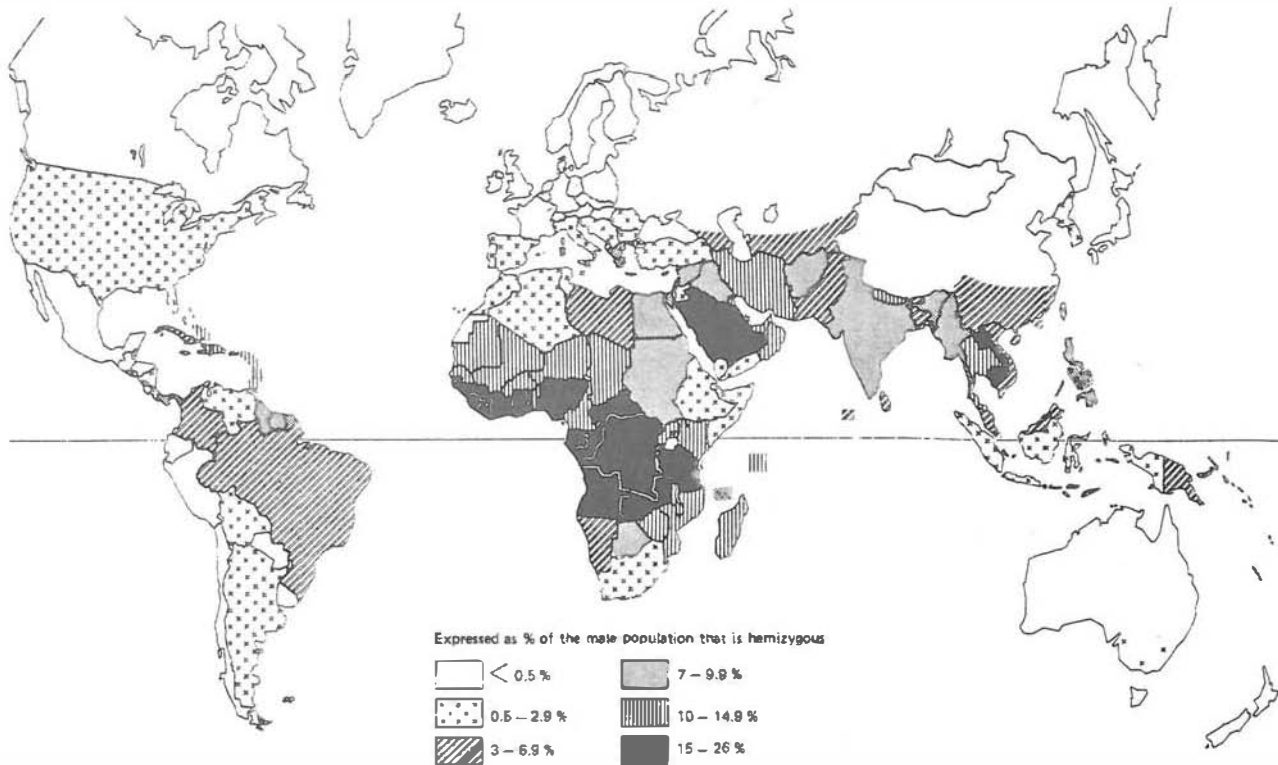


Fig. 1. World distribution of G6PD deficiency. With courtesy from the "WHO working group, Bulletin 1989".

deficiency being expressed in the liver, and type II which is a rarer, frankly hemolytic type.<sup>6</sup>

Most neonates (group I) developed NNJ type II with anemia (Table III). Sepsis, prematurity, hypoxia and acidosis were associated with this type of NNJ.

It is possible that hydrogen peroxide released from phagocytic cells during infection<sup>10</sup> leads to hemolysis in neonates. However, hemolysis triggered by infection is characteristically mild.<sup>5</sup>

Although certain drugs, fava beans, and oxidative substances can cross the placenta or are excreted into breast milk, causing NNJ type II and rarely erythroblastosis fetalis,<sup>3,10</sup> only one neonate whose mother had consumed cotrimoxazole developed hemolysis.

Immature neonates are especially susceptible to NNJ type II because of relative vitamin E deficiency, elevated vitamin C levels, glutathione peroxidase and catalase decrement and red blood cell lifespan shortening.<sup>1,11</sup> 3 of our neonates (16.6%) were premature with no other predisposing factors except for prematurity. Chronic anemia in 3 children (6.2%) of group II suggests CNSHA as an uncommon manifestation of the disease.

Comparing available statistics for blood group distribution in the population [O=36.72%, A=31.58%, B=24.19% and AB=7.51%]<sup>8</sup> with our children (Table III), enzyme deficiency is more likely to develop in blood group

O ( $p < 0.01$ ).

77.7% of neonates and 79.1% of children had blood transfusions and, regarding the complications of transfusion, performing a screening

WHO, neonatal screening should be performed on cord blood samples in populations where G6PD deficiency is common (i.e. where it affects more than 3-5% of males) whenever possible in order to monitor these vulnerable infants for jaundice and institute treatment as early as possible.<sup>2,4</sup> of our neonates (22.2%) with kernicterus survived and one child (1.5%) died because of severe anemia accompanied by uncontrollable viral encephalitis.

According to WHO, in developing countries where G6PD deficiency is common and screening facilities are not available, simple recommendations could be forwarded for early identification of patients.<sup>2</sup>

Since no epidemiological study of the disease has been conducted in our country, the results of our pilot study recommend that a screening test be performed in conditions such as neonatal jaundice, males who have blood group O, a positive family history of the disease and children hailing from northern and western parts of Iran.

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