

# Does the history before blood transfusion identify donors who are glucose-6-phosphate dehydrogenase (G-6-PD) deficient?

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## ABSTRACT

The incidence of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency in Iran is around 10-14.9%. G-6-PD deficiency is an X-linked recessive disorder that is more prevalent in males. In our area, 80% of blood donors are males. At present, pre-donation data are relied on for detecting diseases in Shiraz blood banks and the donors' blood is not routinely screened for G-6-PD deficiency. Transfusion of such blood may induce hemolysis in recipients, especially in premature neonates and in neonates having exchange transfusion.

Four hundred and fifty blood bags in a blood bank of Shiraz from male donors were enrolled in this cross-sectional study. The blood samples were tested with fluorescent spot test for G-6-PD deficiency. G-6-PD-deficient donors were identified, and if they agreed, were asked to participate in the study. Each volunteer filled out a questionnaire.

From 450 blood bags, 27 bags were G-6-PD deficient (6%). Only 19 donors could be traced who volunteered to participate in the study. Two donors (10%) had positive past history of hemolysis. Ten donors (52.6%) had positive family history of hemolysis (red urine and jaundice) when exposed to fava beans, mothballs, aspirin or other drugs. Nine donors had a male member in the family with hemolysis and one had a female relative with hemolysis. Five donors (26.3%) had positive history of neonatal jaundice.

According to this study, 52% of donors had a positive family history of hemolysis, but only 10% had positive history of hemolysis themselves; therefore, addition of past history and family history of hemolysis has a good predictive value in detection of the G-6-PD-deficient donors.

**Key Words:** Blood transfusion, glucose phosphate dehydrogenase deficiency, hemolysis

## INTRODUCTION

Glucose-6-phosphate dehydrogenase (G-6-PD) deficiency is the most common known human enzyme deficiency, affecting 10% of the world's population, and it accounts for 200 to 400 million affected people worldwide<sup>[1]</sup>. Deficiency of G-6-PD in the red blood cells, under certain circumstances, could lead to an abnormal rupture of the cell wall with resultant hemolytic anemia. The likelihood of developing hemolysis and its severity are determined by the magnitude of the enzyme deficiency, which is relevant to the biochemical characteristics of each G-6-PD variant. On this basis, the World Health Organization (WHO) has classified the different G-6-PD variants<sup>[2]</sup>.

The abnormal gene responsible for this inherited deficiency is located on the X chromosome. Therefore, the illnesses associated with G-6-PD deficiency occur more frequently in males than females<sup>[3]</sup>. With the most prevalent G-6-PD variants (G-6-PD A- and G-6-PD Mediterranean), hemolysis is induced by sudden destruction of the older and more deficient erythrocytes, which happens after exposure to some drugs of high redox potential, mothballs, henna, fava beans, or with certain infections and metabolic abnormalities. In G-6-PD-deficient neonates, decreased bilirubin elimination may play an important role in development of jaundice<sup>[4,5]</sup>.

Considering the potential hazards of severe hemolysis in neonates, and also since 80% of the donors are males, this study was conducted to determine if addition to pre-donation questionnaire forms of hemolysis history due to fava beans in donors or their families and previous history of hemolysis by aspirin or other drugs would be helpful in detection of the G-6-PD-deficient donors.

## MATERIALS and METHODS

In this cross-sectional study, 450 male donor blood bags from a blood bank of Shiraz were selected. The samples were tested for G-6-PD deficiency by fluorescent spot test. Deficient donors were identified and the following questions were asked from those who volunteered to take part in the study:

1. Do you have any history of red urine or jaundice (hemolysis) after ingesting fava beans, aspirin, nalidixic acid or trimethoprim sulfamethoxazole or other drugs?
2. Does any member of your family have a history of red urine or jaundice (hemolysis) after ingesting fava beans, aspirin, nalidixic acid or trimethoprim sulfamethoxazole or other drugs?
3. Is there any history of favism in your family members?
4. Do you have any history of neonatal jaundice?
5. Do you have any history of exchange transfusion for neonatal jaundice?

## RESULTS

From 450 male donor samples, 27 (6%) were G-6-PD deficient; all of them had negative history of jaundice or hepatitis.

Only 19 donors could be traced and volunteered to participate in the study.

Two donors (10%) had positive past history of hemolysis. Ten donors (52.6%) had positive family history of hemolysis (red urine and jaundice) when exposed to fava beans, mothballs, aspirin or other drugs. Nine donors had a male member in their family with hemolysis and one had a female relative with hemolysis. Five donors (26.3%) had positive history of neonatal jaundice. Results are shown in Table 1.

**Table 1.** Questionnaire results

Question	Positive response/total	Percent
Do you have a history of red urine or jaundice (hemolysis) after ingesting fava beans, aspirin, nalidixic acid or trimethoprim sulfamethoxazole or other drugs?	2/19	10%
Does any member of your family have a history of red urine or jaundice (hemolysis) after ingesting fava beans, aspirin, nalidixic acid or trimethoprim sulfamethoxazole or other drugs?	10/19	52%
Do you have a history of favism in your family?	10/19	52%
Do you have a history of neonatal jaundice?	5/19	26%
Did you have a history of exchange transfusion for neonatal jaundice?	0/19	0%

## DISCUSSION

The first study on prevalence of G-6-PD deficiency in Iranians, done in 1959 on medical staff, showed an incidence of 9.5%<sup>[6]</sup>. Another study on cord blood reported a prevalence of 12% G-6-PD deficiency in males and 0.9% in females in Fars province<sup>[7]</sup>.

According to a WHO report, the overall incidence of G-6-PD deficiency among the Iranian population is 10-14.9%<sup>[8]</sup>. Screening of the donors' blood is not routinely performed, since there are generally no deleterious consequences in recipients of G-6-PD-deficient blood<sup>[9]</sup>. Under normal circumstances, G-6-PD deficiency is harmless in most children. However, it can raise a serious problem in neonates in particular, when they develop an infectious illness or are exposed to certain materials and drugs which increase the amount of oxidative stress on the walls of red blood cells<sup>[3,9]</sup>. Transfusion of G-6-PD deficient red cells to premature infants has been associated with hemolysis and severe hyperbilirubinemia requiring exchange transfusion<sup>[10]</sup>. In addition, massive intravascular hemolysis has also occurred after an exchange transfusion with G-6-PD-deficient blood<sup>[11,12]</sup>.

G-6-PD can be assayed by the classic method of Horecker and Smyrniotis<sup>[13]</sup>, which directly

measures the rate of formation of NADPH. Other methods for G-6-PD screening such as methemoglobin reduction<sup>[14]</sup> and fluorescent spot tests<sup>[15]</sup> are semi-quantitative, and classify a sample simply as normal or deficient, when it has less than 30% of the normal enzyme activity. Above this level one is unlikely to encounter clinical manifestations. The fluorescent spot test used in this study is the simplest, most reliable and most sensitive of the G-6-PD screening tests, which is based upon the fluorescence of NADPH after addition of glucose-6-phosphate and NADP to hemolysate of the test cells<sup>[15,16]</sup>.

All blood samples examined in this study were less than seven days old. Age of red cells is important because during blood storage, glutathione-dependent antioxidant systems in erythrocytes and antioxidant defense in plasma are depleted. Previous studies have shown a twelve-day period as a safe storage limit<sup>[17]</sup>.

This study showed that addition of family history of red urine or jaundice (hemolysis) after ingesting fava beans, aspirin, nalidixic acid or trimethoprim sulfamethoxazole or other drugs to pre-donation questionnaire forms can detect about 52% of G-6-PD-deficient donors, and this is suggested as a very helpful and easy preventive method.

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