Hemolysis Induced by Glucose-6-Phosphate Dehydrogenase Deficiency and Its Association with Sex in Children

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Abstract

Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzyme disorder in human. The aim of this study was to determine the prevalence of G6PD deficiency among children and evaluate its association with ABO/Rh blood groups.

Method: Blood samples of 3401 asymptomatic children were analyzed and compared with 317 children who were admitted to hospital because of hemolysis resulted from G6PD deficiency.

Results: Among asymptomatic children 375 (11%) were G6PD deficient. Male to female ratio for this group was 4.2:1 and for the hemolytic group was 2.5:1 (P=0.004). Two hundred and sixty-seven (84.2%) of the patients with hemolysis were younger than 2 years, with the peak age of hemolysis between 2 and 3 years (27.7%). The overall rate of hemolysis caused by G6PD deficiency was 12.3% during the 3 consecutive months of fresh Fava bean consumption. Blood groups O+, A+, and B+ together constituted 87.1%, 87.7%, and 84% of the blood groups among normal children, asymptomatic G6PD deficient subjects, and those with G6PD deficiency related hemolysis respectively (P=0.367). Seven percent of the normal children and asymptomatic G6PD deficient subjects were Rh- vs 9.7 % of G6PD deficient children with hemolysis (P=0.16).

Conclusion: The prevalence of G6PD deficiency among the children was 11%. Male to female ratio was greater in non-hemolytic vs hemolytic group so that the female share was higher in hemolytic group than in the other two groups (P=0.004).

The distribution of ABO blood groups was similar among asymptomatic non-G6PD deficient, asymptomatic G6PD-deficient, and G6PD-deficient children with hemolysis. The distribution of Rh- types among the G6PD-deficient children with hemolysis and the other two groups was similar (9.7% vs 7%, P=0.16).


Keywords ● Glucose-6-phosphate dehydrogenase ● enzyme ● RBC

Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzyme disorder in human affecting more than 400 million people worldwide.1,2
G6PD is a highly polymorphic enzyme encoded by a human X-linked gene (Xq2.8). This enzyme catalyses the first step of pentose phosphate pathway, which converts glucose 6-phosphate to 6-phosphogluconate with production of NADPH. The deficient cell is vulnerable to oxidative injury to membrane and cytoplasmic proteins. The main clinical manifestations of G6PD deficiency are acute hemolytic anemia and jaundice, triggered by infection or ingestion of Fava beans or oxidative drugs. A variant of G6PD, named Mediterranean, is the most frequent allele found among patients in Southern Iran. And is often associated with favism. The relationship between G6PD deficiency and ABO/Rh blood group is still controversial. The aim of the present study was to review the epidemiologic aspects of G6PD deficiency (with or without hemolysis) among asymptomatic outpatient and inpatient children with Favism in Southern Iran and to find an association with ABO, or Rh blood groups.

Patients and Methods

During a 9-year period (1994-2003), tests for ABO blood groups, Rh typing, and G6PD activity were conducted on 3401 children in Shiraz (south of Iran). All the children were Muslim and selected randomly among the visitors of the first author’s (E.S) outpatient clinic. The included children were asymptomatic children aged 1-14 years referring for routine checkup, with no history of hemolysis, and with normal blood count and peripheral smear. Informed consents were obtained from the parents. Blood samples were drawn in the early morning with EDTA anticoagulant. G6PD activity assay was performed in a clinical laboratory affiliated to Shiraz University of Medical Sciences, using dye reducing (Brilliant cresyl blue) test and carried out on 0.1 ml of hemolysed blood. Blood group and Rh typing were also performed on the samples at the same time.

In addition, we reviewed hospital records of 317 G6PD deficient patients with hemolysis, among a total of 2567 patients, who admitted to the Pediatric Emergency Department of Nemazee hospital affiliated to the same University during the season of heavy Fava bean consumption (April, May, and June) in years 1996 to 1998. Blood group and Rh were found in records of 226 of these patients.

Data were analyzed by Chi-square test using SPSS software (version 12.0) for the PC, (SPSS Japan Inc, Tokyo). A P value of less than 0.05 was considered statistically significant.

Results

Of the 3401 children visited in outpatient clinic, 375 (11%) were G6PD deficient. There were 304 (81%) male and 71 (19%) female patients with the male to female ratio of 4.2:1. There were 317 (12.3%) G6PD deficient children with hemolysis among 2567 children admitted to the Emergency Department in the three months of fresh Fava bean consumption period. Of them, 228 (72%) were male and 89 (28%) were female patients, with male to female ratio of 2.5 to 1. There were more females in this group compared with the G6PD deficient children in the outpatient group (P=0.004). The monthly distribution of G6PD deficiency related hemolysis in fava bean consumption season is shown in table 1 and figure 1.

Figure 2 depicts the age distribution of the patients with hemolysis. Most (84.2%) of the patients admitted to the Emergency Department with G6PD deficiency related hemolysis, were younger than five years old. The peak age of hemolysis was between 2 and 3 years (27.7%).

G6PD deficiency related hemolysis began with a sharp increase in April, gradually decreased in May and declined to the lowest point in late June, as the fresh Fava bean consumption period ended. No case of G6PD deficiency related hemolysis caused by Fava bean consumption was reported during the remaining 9 months of the years. Although the frequency of hemolysis almost doubled for the corresponding months of 1997 compared with 1996, the rate of decline was similar for the corresponding months of the consecutive years.

The results of blood groups and Rh typing performed on asymptomatic children and those with G6PD deficiency related hemolysis are shown in table 2. The patients with partially deficient G6PD are not included in the table 2. Blood groups of O+, A+, and B+ together constituted 87.1%, 87.7%, and 84% of the blood groups among normal children, asymptomatic G6PD.
deficient children, and those with G6PD deficiency related hemolysis, respectively (P=0.367).

The O* type was the most prevalent blood group among all the study participants, ranging from 37.5-40%, followed by A* type (25-26%), B* type (20-23.6%), and AB* type (5-6%). In addition, 7% of the normal and asymptomatic G6PD deficient children were Rh* (P=0.16). There were

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**Table 2:** The distribution of blood groups and Rh factor among normal children, G6PD-deficient asymptomatic children and patients with G6PD deficiency related hemolysis admitted to Nemazee Hospital

<table>
<thead>
<tr>
<th>Blood Group</th>
<th>Normal children</th>
<th>Asymptomatic</th>
<th>G6PD Deficient</th>
<th>With hemolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh*</td>
<td>2808 (92.8%)</td>
<td>218 (7.2%)</td>
<td>348 (92.8%)</td>
<td>27 (9.7%)</td>
</tr>
<tr>
<td>Rh-</td>
<td>218 (7.2%)</td>
<td>218 (7.2%)</td>
<td>27 (9.7%)</td>
<td>22 (9.7%)</td>
</tr>
</tbody>
</table>

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**Figure 1:** Cumulative monthly distribution of G6PD deficient patients in three consecutive years (1996-98).

**Figure 2:** Age distribution of children referred to Emergency Department with G6PD deficiency related hemolysis.
more Rh- types among the G6PD deficient pa-
tients who developed hemolysis compared with
the other two groups but this difference was not
statistically significant (9.7% vs 7%; P=0.16).

Discussion

G6PD deficiency is the most common meta-
bolic disorder of red blood cells, involving more
than 400 million people worldwide. It is more
prevalent in the tropical and subtropical areas
of the Eastern hemisphere (where, as high as
35% of the population may be affected). The
prevalence of G6PD deficiency may vary in
different parts of the world. Frischner and col-
leagues in 1973 found a prevalence of 10.6%
in African-Americans, 9.8% in Iranians, 4.1% in
South Vietnamese, and 0.5% in Ethiopians. Other
studies revealed the frequency of G6PD
deficiency, 4.3-6% in different population
groups of Assam, 5.2% in Greece, 0.3% in
northern and 2.2% in southern Italy, 8% in
Somalis, and 11.4% in male and 2.5% in fe-
male African-American infants. The fre-
quency of G6PD deficiency may vary among
different ethnic groups of a population as well.
Study by Hedayat and co-workers in Iran,
showed the prevalence of G6PD deficiency to
be 9.94% for Moslems, 15.23% for Jews, and
13.39% for Armenians. Frequencies of G6PD
deficiency has been reported to be higher in
Kurdish Jews than those in any other ethnic
population.

The present study showed that the overall
prevalence of G6PD deficiency among the Mos-
lem children of Shiraz is 11% and remained
unchanged when it was monitored repeatedly
during a course of 9-year study period. This fig-
ure is close to the prevalence rate achieved by
some other studies in Southern Iran.

Two recent studies in Iran showed that the
frequencies of G6PD Mediterranean were
84.6% in Fars province (southern Iran) and
66.2% in Mazandaran province (northern Iran).
The molecular characterization of G6PD defi-
ciency in Fars province of Iran is similar to the
finding in United Arab Emirates, and
Southeast Asia. The male to female ratio, although may dif-
ferr in various regions and ethnic groups, remained unchanged during the course of our
study. This ratio for the patients with Favism
(hemolytic group) was 2.5:1. The female share
was higher in hemolytic group than in asym-
tomatic G6PD-deficient group, with a signifi-
cant statistical difference (P=0.004). It might be
resulted from the fact that females have to
inherit two X genes to present with G6PD
manifestations. However, acqirement of two
defective genes may result in more severe
clinical manifestations.

Most of our patients admitted to Emergency
Department with G6PD deficiency related
hemolysis, were younger than five years old. The
peak hemolysis occurrence age was between
the ages of 2 and 3 years. Study by Hedayat
and colleagues in the Caspian littoral area
(north of Iran) also showed the peak of Favism
occurrence at the age of 2-3 years. Therefore,
among our patients, those at pre-school
age (2-5 years) seemed to be the most vulner-
able for G6PD related hemolysis.

The distribution of ABO and Rh blood groups
was quite similar among asymptomatic G6PD-
deficient and non-G6PD-deficient children. The
same result was also reported by Lesho. However,
in contrary to Tzoneva and colleagues, we
found Rh- more frequently among patients
with hemolysis than asymptomatic or non-
G6PD-deficient children; although the difference
was not significant (P=0.16).

It might be concluded that G6PD defi-
ciency-related hemolysis could relatively be
more common among the female patients. Fur-
ther studies in the endemic areas are recom-
ended to find the possible causes.

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Conflict of Interest: None declared

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