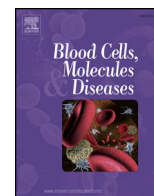




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## Favism, the commonest form of severe hemolytic anemia in Palestinian children, varies in severity with three different variants of G6PD deficiency within the same community



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## ABSTRACT

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common genetic abnormality known to predispose to acute hemolytic anemia (AHA), which can be triggered by certain drugs or infection. However, the commonest trigger is fava beans (*Vicia faba*) ingestion, causing AHA (favism), which may be life-threatening especially in children. G6PD deficiency is genetically highly heterogeneous, as nearly 200 different mutations have been observed. We have investigated the hematological features of acute favism in the Palestinian Gaza community that is characterized by the polymorphic coexistence of three different G6PD deficiency genes (*G6PD A-*, *G6PD Cairo*, *G6PD Med*). We have found by comparison to the general population (485 adults and 466 newborns) that children with favism, in terms of relative frequency, *G6PD A-* was under-represented, whereas *G6PD Med* was over-represented. We also found that the severity of anemia was significantly greater with *G6PD Med* and *G6PD Cairo* than with *G6PD A-*; and with *G6PD Cairo*, compared to the other two variants, there was greater hyperbilirubinemia, as well as persistence of mild anemia and reticulocytosis for as long as 4 months after recovery from favism. This is the first report determining a differential impact of different G6PD mutations on the clinical features of favism in the same population and the same environment.

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## 1. Introduction

Favism (OMIM 134700) was recognized for over a century as a form of acute hemolytic anemia (AHA) that is life-threatening especially in children [1]. Once glucose-6-phosphate dehydrogenase (G6PD; EC

1.1.1.49) deficiency was discovered [2], it became clear that G6PD deficiency was an essential inherited predisposition to develop favism [3]. Initially favism was characterized particularly in Greece [4], Italy [5], and in the Middle East [6]; but subsequently also in North Africa, Thailand, China, and in some 30 other countries (listed in [7]). With appropriate management, which often must include blood transfusion, full recovery from favism without sequelae is the rule [8]; however, if not promptly diagnosed and managed it is still a life-threatening condition.

The *G6PD* gene (OMIM 305900) maps to the sub-telomeric region of the long arm of the X chromosome (band Xq28). G6PD deficiency, which is therefore X-linked, is well known to be highly heterogeneous at the genetic level, since different mutations underlie different variants, many of which have polymorphic frequencies in areas where malaria is or has been endemic [7]. G6PD deficiency is never complete: nearly all G6PD mutations are missense mutations or in-frame deletions [9], and all have some residual G6PD enzyme activity; indeed, a classification

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