The Preterm Infant

A High-Risk Situation for Neonatal Hyperbilirubinemia Due to Glucose-6-Phosphate Dehydrogenase Deficiency

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KEYWORDS

• Glucose-6-phosphate dehydrogenase deficiency • Prematurity • Hyperbilirubinemia • Kernicterus • Bilirubin encephalopathy • Hemolysis • Bilirubin conjugation

KEY POINTS

- Glucose-6-phosphate dehydrogenase (G6PD) deficiency can be associated with sudden and acute episodes of unpredictable, severe, or extreme hyperbilirubinemia.
- Immaturity of the bilirubin conjugating system in preterm infants may exacerbate hyperbilirubinemia by slowing the bilirubin excretory process.
- Both prematurity and G6PD deficiency are independent risk factors for neonatal hyperbilirubinemia, and together they can act synergistically with the potential for bilirubin encephalopathy and kernicterus.
- Preterm infants and infants with hemolytic conditions are thought to be at increased risk for bilirubin neurotoxicity compared with term infants or those without hemolysis.
- Early screening for G6PD deficiency and vigilant observation for jaundice, both in hospital and after discharge home, should facilitate referral to a medical center before the development of acute bilirubin encephalopathy.

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Box 1
Some population subgroups in North America with a high frequency of glucose-6-phosphate dehydrogenase deficiency relative to the background frequency

African American

Sephardic Jews (Middle Eastern origin)

Mediterranean Basin (Italy, Greece, Turkey, Syria)

Middle Eastern origin

India

China

INTRODUCTION

Glucose-6-Phosphate Dehydrogenase Deficiency and Prematurity as Coexisting Risk Factors for Neonatal Hyperbilirubinemia

Glucose-6-phosphate dehydrogenase deficiency: the scope of the problem

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most frequent enzyme deficiency encountered in humans and is estimated to affect more than 300 million individuals worldwide.[1,2] No longer limited to its indigenous distribution, which included the Mediterranean Basin, Central and West Africa, the Middle East, and Asia, slave trade, migration patterns in the past and present, and current-day ease of travel have transformed G6PD deficiency into a potentially dangerous condition that can be encountered in virtually any corner of the globe. Not surprisingly, G6PD deficiency is an important contributor to severe hyperbilirubinemia and kernicterus in low- and middle-income, developing countries with a high frequency of the condition.[3] Even more disturbing is the fact that G6PD deficiency features prominently in series of newborns with bilirubin neurotoxicity reported from Western countries, which have developed and functional health care systems, including the United States, Canada, the United Kingdom, and Ireland.[4–6] Complacency on the part of health care workers that, because they live in a geographic area with a low indigenous frequency of G6PD deficiency and the condition is of no concern to them, is no longer valid. Although North America is regarded as a low G6PD-deficiency region (0.5% to 2.9% male incidence in the United States and <0.5% in Canada),[7] there are subgroups of the population with a high frequency and whose members are at increased risk for the potential complications of the condition. At the top of this list are African Americans, in whom the male frequency of G6PD deficiency is 11% to 13% (**Box 1**).[8]

Medical complications associated with glucose-6-phosphate dehydrogenase deficiency

Favism and acute hemolytic episodes Most G6PD-deficient individuals will lead completely normal lives and, unless tested for, be unaware that they have the condition (**Box 2**). Some foods, chemical substances, and drugs may contain oxidizing

Box 2
Main potentially dangerous medical conditions associated with glucose-6-phosphate dehydrogenase deficiency

- Favism
- Extreme neonatal hyperbilirubinemia with potential for bilirubin neurotoxicity
- Moderate neonatal hyperbilirubinemia