Glucose-6-Phosphate Dehydrogenase Activity Levels in White Newborn Infants

Alissa N. Doherty, MD[1], Elizabeth A. Kring, RN[1], Yvonne F. Posey, MD[2], and M. Jeffrey Maisels, MBBCh, DSc[1]

Objective To define normal levels of glucose-6-phosphate dehydrogenase (G6PD) activity in a population of North American white newborns.

Study design We studied 2 white newborn populations, ≥35 weeks of gestation. In the retrospective study, G6PD activity was measured (on clinical indication) in 242 newborns aged ≤7 days. In the prospective study, we measured G6PD activity in umbilical cord blood samples in 347 newborns and daily transcutaneous bilirubin levels in these infants.

Results The mean G6PD activity level was 12.3 ± 3.1 units per gram hemoglobin (U/gHb) in the retrospective population and 13.3 ± 1.8 U/gHb in the prospective population, and there was no difference between males and females. The distribution of values suggested that infants with activity levels <7 U/gHb should be considered deficient and 8 infants (6 males and 2 females), all in the retrospective population had such levels.

Conclusions As in other ethnic populations, the mean G6PD activity in white newborn infants is substantially greater than that of white adults. The lower limits of normal are also similar to those of other newborn ethnic groups and of adults. The diagnosis of G6PD deficiency should be considered in any white infant whose G6PD activity is <7 U/gHb. *(J Pediatr 2014;164:1416-20)*.

Glucose-6-phosphate dehydrogenase (G6PD) deficiency, the most common enzymatic defect in the world, affects an estimated 400 million people.[1] In the newborn infant, G6PD deficiency is an important cause of hemolytic anemia and hyperbilirubinemia[2] and was the putative cause of extreme hyperbilirubinemia in 21% of infants in the US kernicterus registry[3] and 25% of those diagnosed with chronic bilirubin encephalopathy in Canada.[4]

African American and Middle Eastern newborns have levels of G6PD activity that are significantly higher than those seen in adults[5-7] but no similar data exist for a population of Caucasian infants. Because our clinical laboratory (and many others) provides normal reference ranges based on adult G6PD activity, we believed it important to define normal levels of G6PD activity in a population of North American white newborns on the assumption that the use of adult levels could result in a missed case of G6PD deficiency in these infants.

Methods

We measured G6PD activity in 2 populations of white newborn infants ≥35 weeks of gestation. Infants were identified as white by their mothers' self-reported race/ethnicity at the time of registration or from the newborn screening record. In our first, retrospective study, we used the laboratory computer database to identify G6PD levels measured on clinical indication (presumably hyperbilirubinemia), between January 2007 and December 2011, in 242 newborns aged ≤7 days. In the second, prospective study, we used umbilical cord blood samples from 347 white newborn infants born at Beaumont Hospital, Royal Oak, between March and May 2013. Umbilical cord blood gases are routinely measured in all newborns, and a sample for G6PD activity was collected at the same time as the blood gas sample. Beaumont Health System's Institutional Review Board approved both studies and did not require parental permission for the prospective study, but mothers were provided with a written explanation of the study and were offered the option of refusing to participate, in which case the sample for G6PD activity was discarded. We enrolled healthy, nondistressed neonates, ≥35 weeks of gestation. We excluded infants with significant distress, congenital anomalies, or if the sample was inadequate.

G6PD activity was measured using a commercial kit (Trinity Biotech, Jamestown, New York). This procedure is standardized on the basis that nicotinamide adenine dinucleotide phosphate light absorbance, measured at a wavelength of 340 nm, has a known millimolar extinction coefficient of 6.22. The oxidation of glucose-6-phosphate to 6-phosphogluconate, catalyzed by G6PD, leads to reduction of nicotinamide adenine dinucleotide phosphate+ to nicotinamide adenine

G6PD	Glucose-6-phosphate dehydrogenase
TcB	Transcutaneous bilirubin
U/gHb	Units per gram hemoglobin

From the [1]Department of Pediatrics, Oakland University William Beaumont School of Medicine, and Beaumont Children's Hospital; and [2]Department of Pathology and Laboratory Medicine, Oakland University William Beaumont School of Medicine and Beaumont Health System, Royal Oak, MI

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Table I. Patient demographics in the retrospective and prospective study populations

	Retrospective	Prospective	Totals
Sex			
Male	130 (53.7%)	194 (55.9%)	324 (55%)
Female	112 (46.3%)	153 (44.1%)	265 (45%)
Gestational age			
35-36 6/7 wk	44 (18.2%)	13 (3.8%)	57 (9.7%)
37-38 6/7 wk	85 (35.1%)	75 (21.6%)	160 (27.2%)
39-40 + wk	113 (46.7%)	259 (74.6%)	372 (63.1%)

dinucleotide phosphate on a molar equivalent basis. Therefore, measurement of the rate of increase in absorbance at 340 nm allows quantification of enzymatic activity. Absorbance was measured by the Beckman DU 730 Spectrophotometer at 30°C and hemoglobin was measured on each sample with the Sysmex XE-5000 (Siemens Medical Solutions USA, Inc, Malvern, Pennsylvania). G6PD enzyme activity was reported as units per gram hemoglobin (U/gHb).

In the prospective study, per hospital protocol, we performed transcutaneous bilirubin (TcB) measurements daily

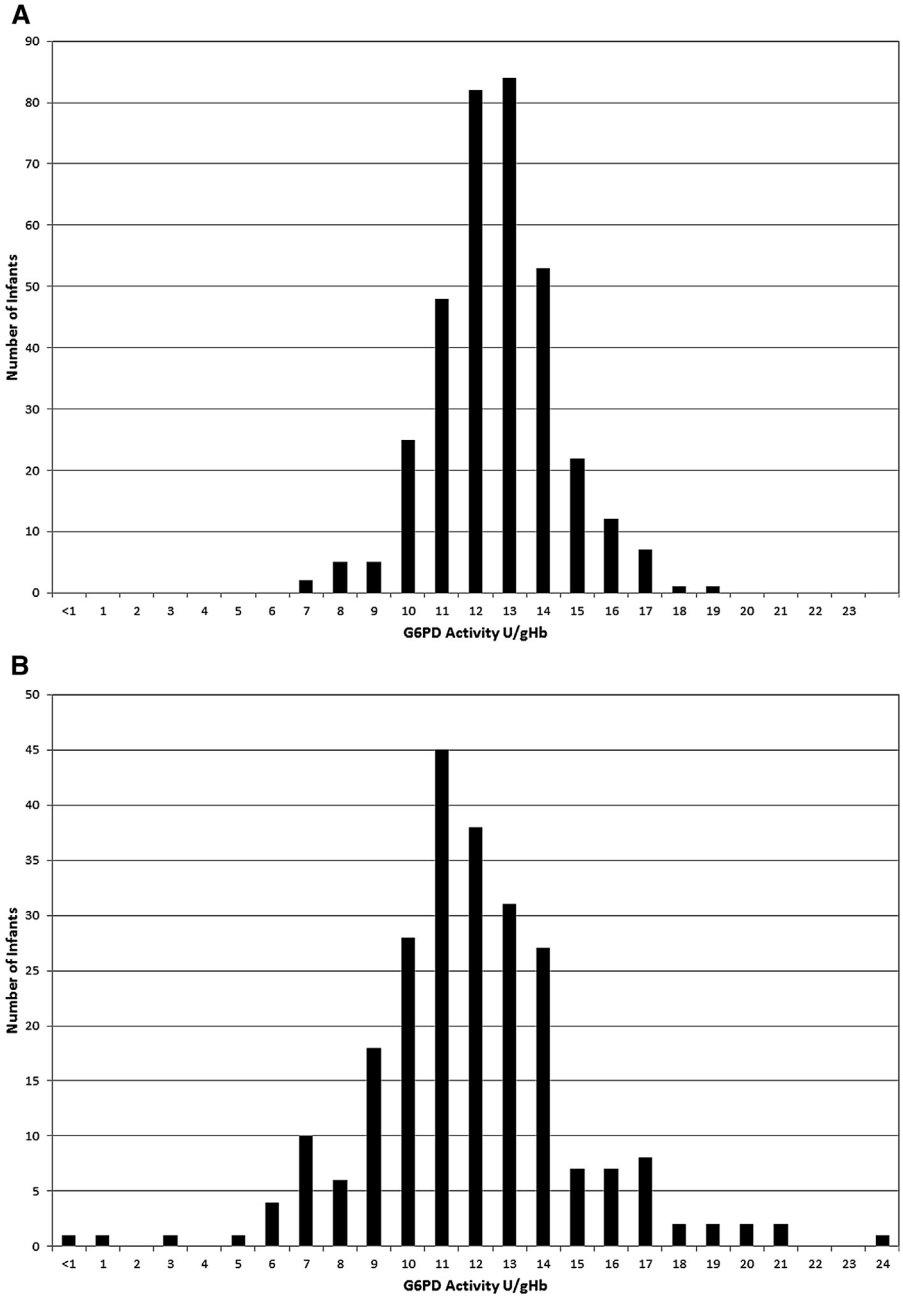

Figure 1. G6PD activity distribution in the **A,** prospective population (n = 347) and **B,** retrospective population (n = 242).