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Original Article

Prevalence of glucose-6-phosphate dehydrogenase (G6PD) deficiency in neonates in Bunda Women's and Children's Hospital, Jakarta, Indonesia

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Abstract

Background Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzyme deficiency in the world. It is a risk factor for hyperbilirubinemia in neonates, which can cause serious complications such as bilirubin-induced encephalopathy or kernicterus. WHO recommends universal neonatal screening for G6PD deficiency when the frequency exceeds 3-5% of male newborns.

Objective To assess the prevalence of G6PD deficiency among neonates in Bunda Women and Children Hospital (Bunda WCH), Jakarta, in order to determine if there is a need for routine G6PD neonatal screening.

Methods This is a cross-sectional and retrospective study; infants' data were obtained from medical records. From January 2009 to May 2010, all neonates in Bunda WCH were screened for G6PD deficiency on the 3rd day of life. Blood samples were collected using filter papers. We considered a result to be normal if it exceeded 3.6 U/g Hb.

Results A total 1802 neonates were screened. We found 94 neonates (5.2%) with G6PD deficiency. Out of 943 males, 59 (6.26%) were G6PD deficient, and out of 859 females, 35 (4.07%) were G6PD deficient. We observed that prevalence of G6PD deficiency according to sex distribution was significantly higher in males than females (6.26% vs. 4.07%, P=0.037). There was no significant difference in the risk for severe hyperbilirubinemia between the G6PD deficient infants and the normal infants (P=0.804).

Conclusions The frequencies of G6PD deficiency were 6.26% of male neonates and 4.07% of female neonates. We recommend universal neonatal screening for G6PD deficiencies in Jakarta since our findings exceed the WHO recommendation for routine testing. **[Paediatr Indones. 2011;51:29-33]**.

Keywords: *G6PD, screening, prevalence, neonates, Jakarta, Indonesia*

G6PD (glucose 6-phosphate dehydrogenase) deficiency is the most common enzyme deficiency in the world.[1] Nkhoma *et al* estimated that 330 million people in the world are affected by G6PD deficiency and global prevalence is about 4.9%.[2] Prevalence of G6PD deficiency varies according to the ethnicity in populations.[3] Usually G6PD deficiency occurs in Mediterranean, African, Southeast Asian, South European, Middle Eastern and Oceanic regions, with an incidence as high as 25% in some populations.[1,4] The prevalence of severe G6PD deficiency in reached 2.2% Turkey[5], 0.8% in Iran[3] and 7.9% in Southern Brazil[6]. We predicted a high incidence of G6PD deficiency in Indonesia, since it is in Asia, one of the highly affected regions. There have only been a few studies about G6PD deficiency in Indonesia, especially in Jakarta. The prevalence of G6PD deficiency was as high as 14% among males in Semarang, Central Java[7], 6.2% among males in Flores[8], 5.9% among males in three Flores ethnic populations (Sikka, Ende

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and Bajo)[9], and 8% among males in Sumba Island, Indonesia[10].

Mohammadzadeh *et al* found that G6PD deficiency in Iran is more likely to occur in males (1%) than in females (0.5%), with gender breakdown of 69.4% males and 30.6% females ($P < 0.05$).[3] But Castro *et al* stated that the gender difference of G6PD deficiency was not statistically significant ($P=0.101$).[6] Furthermore, Kawamoto *et al* found the prevalence of G6PD deficiency to be higher in females than males among the Ende population.[9] G6PD deficiency is one of the risk factors for hyperbilirubinemia in neonates.[11,12] In neonates, severe hyperbilirubinemia can cause serious complication such as bilirubin induced encephalopathy or kernicterus.[13] Johnson *et al* found that 20-30% of reported kernicterus cases in the United States were related to G6PD deficiency.[14] Slusher *et al* found that infants with kernicterus had a higher prevalence of G6PD deficiency than those without kernicterus (75% versus 22%). They also observed that subjects with G6PD deficiency had a higher level of Total Serum Bilirubin (TSB) than normal subjects ($P=0.004$).[15] Early detection of G6PD deficiency may prevent or reduce morbidity because patients can receive timely information on drugs, foods, and other substances that can induce clinical manifestations.[15]

From early 2009, G6PD screening on neonates in their third day of life has been a protocol in Bunda WCH, Jakarta. The screening method used was a quantitative test of enzymatic activity. Currently, only a few countries in the Asia Pacific region have G6PD screening programs, including Singapore, Malaysia, Philippines and Taiwan.[16] WHO recommends universal G6PD screening if the frequency of G6PD deficiency exceeds 3-5% in males.[17] In Indonesia, we did not have the standard protocol for G6PD screening in neonates. The aims of this study were to determine the prevalence of G6PD deficiency, and the risk of severe hyperbilirubinemia in G6PD deficient infants, according Bhutani's normogram.[19]

Methods

This was a cross-sectional and retrospective study to determine the prevalence of G6PD deficiency in neonates in Bunda WCH, Jakarta, Indonesia. The infants' data were obtained from medical records. During the period of January 2009 to May 2010 neonates in Bunda WCH were screened for G6PD deficiency. Infants were excluded from this study if we did not have the results of G6PD screening test. On the third day of life the G6PD screening was performed. Blood samples were collected by using filter papers, and sent to Prodia to be tested by enzyme immunoassay method. The reagent used was from Bio-Rad Laboratories, Berkeley. The dried blood spots were dissolved in buffer solution, followed by incubation in a glucose-6-phosphate and tetrazolium salt solution. G6PD in specimens converted nicotinamide adenine dinucleotide phosphate (NADP) into a reducted form, NADPH. Tetrazolium salt was converted into formazan dye which was detected by kinetic reading (mOD/min) at 570 nm. G6PD activity was measured by multiplying the average mOD/min with a factor. The nominal of the factor can be obtained by dividing the known normal nominal of the control with the average of the normal control. One unit is a total G6PD that catalyzes the formation of 1 μmol NADPH per minute per gram hemoglobin. We considered the result to be normal if it exceeded 3.6 U/g Hb.[18]

The risks of severe hyperbilirubinemia were categorized using Bhutani's normogram.[19] We divided the risk into four groups: high risk zone, high intermediate risk zone, low intermediate risk zone and low risk zone.[22] The data were analyzed by SPSS 15 software. Prevalence was reported as descriptive data in the form of sum and percentage. We analyzed the predisposing factor of gender and the correlation between risk of severe hyperbilirubinemia and G6PD deficiency using the chi square test. Statistical significance was considered to be $P < 0.05$.

Results

Ninety-four out of 1802 neonates screened by a quantitative test of enzymatic activity were found to be G6PD deficient (5.2%). The distribution of G6PD deficiency between males and females is shown below: 59 out of 94 cases were male (62.77%), and 35 out of 94 cases were females (37.23%). There was a significant difference in prevalence of G6PD deficiency between males, 6.26%, and females, 4.07%,

(P=0.037). **(Table 1)**

From 1802 infants, 2 infants did not have total bilirubin serum results. Five infants from the G6PD deficient population were in the high risk zone for severe hyperbilirubinemia, 7 infants in the high intermediate risk zone, 23 infants in the low intermediate risk zone, and 59 in the low risk zone. In normal populations, 69 infants were in the high risk zone, 158 infants in the high intermediate risk zone, 374 infants in the low intermediate risk zone, and 1105 infants in the low risk zone. There was no significant difference between the risk of severe hyperbilirubinemia according to Bhutani's normogram among the G6PD deficient and normal infants (P=0.804). **(Table 2)**

Table 1. Prevalence of G6PD deficiency among neonates

	G6PD deficient	Normal	Percentage	
Male	59	884	6.26%	P=0.037
Female	35	824	4.07%	
Total	94	1708		

Table 2. Risk of severe hyperbilirubinemia according to Bhutani's normogram in the G6PD deficient and normal infants

Bhutani's normogram	G6PD deficient (n)	Normal (n)	
High Risk Zone	5	69	P=0.804
High Intermediate Risk Zone	7	158	
Low Intermediate Risk Zone	23	374	
Low Risk Zone	59	1105	
Total	94	1706	

Discussion

We used the quantitative test of enzymatic activity to detect G6PD deficiency. Although WHO recommends using a fluorescent test, this method is rarely available in our country. Kaplan *et al*. compared the fluorescent test and the quantitative test of enzymatic activity and found similar accuracy in the two assays.[18] According to WHO, 7.5% of the world's population have one or two genes that affect G6PD deficiency, and 2.9% have G6PD deficiency.[17] This G6PD deficiency is more likely to happen in the Mediterranean, Africa, Southeast Asia, South Europe, Middle East and Oceania.[1,4] Nkhoma *et al*. estimated that the highest prevalence of G6PD deficiency occured in the Sub-Saharan region, while Africa and the Middle East have the second highest prevalence. [2]

A few studies on G6PD deficiency in Indonesia revealed varied prevalences. Soemantri *et al*. found the prevalence of G 6PD deficiency among males in Semarang, Central Java as high as 14%.[7] Matsuoka *et al*. found the prevalence of G6PD deficiency as high as 6.2% among males in Flores,[8] while Kawamoto *et al*. found the prevalence was 5.9% among males and 3.6% among females.[9] In a study conducted in Sumba Island, not far from Flores, Shimizu *et al*. found the prevalence reached 8% among males.[10] In our study, we found the prevalence of G6PD deficiency among male neonates in Bunda hospital was 6.26%, similar to the findings of Matsuoka *et al*., but much lower than Soemantri *et al*. [7,8] This result shows the continuing need for G6PD deficiency screening in neonates in Bunda WCH, Jakarta, as recommended by WHO.[17] The prevalence of G6PD deficiency among females in our study was higher than that of Kawamoto *et al*. [9] (4.07% vs 3.6%). The total prevalence of G6PD deficiency among neonates in Bunda WCH, Jakarta was 5.2%.

Male gender is a risk factor for G6PD deficiency. Males are more commonly affected by this disorder than females. [3,5,11,19] In our study we found a significantly higher difference in the prevalence of G6PD deficiency in males than in females (P=0.037). In contrast, Kawamoto *et al*. found a higher prevalence of G6PD deficiency in females in the Ende population, Flores, Indonesia.[9] However, Castro *et al*. observed no significant difference in the prevalence of G6PD deficiency in males and females in Southern Brazil (P = 0.101).[6]

In our study there was no significant difference between the total serum bilirubin in G6PD deficient infants and normal infants (P=0.804), while Nock *et al*. found that G6PD deficient infants were more likely to be in the high risk zone for severe hyperbilirubinemia on Bhutani's normogram (20.5 vs 7%, P<0.001).[20]

In conclusion, the prevalence of G6PD deficiency in neonates in Bunda WCH, Jakarta was 5.2%, with more males affected than females. We suggest carrying out the G6PD screening protocol in neonates in Indonesia.

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