

GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY IN YOGYAKARTA AND ITS SURROUNDING AREAS

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Abstract. Glucose-6-phosphate dehydrogenase (G6PD) is one of the enzymes needed by the erythrocyte to generate ATP from ADP. Deficiency of this enzyme can lead to hemolysis of red blood cells. Being a malaria endemic area, Indonesia possibly has a high incidence of G6PD deficiency. It is estimated that 2-6% of the population are carriers. In 1996, we detected 145 neonates with G6PD deficiency using the formazan ring method. Among the males, 6.2% had moderate and 1.4% had low enzyme activity; females had enzyme activity in the normal range. Using the Sigma kit, Tashimi *et al* in 1995 examined 111 neonates in Yogyakarta, none of which was identified as "deficient". There was no correlation between erythrocyte hemolysis and G6PD enzyme content. Interestingly, using the same Sigma kit, Soro *et al* in 1994 found that among 134 individuals of Batak descent, 10 males (43.48%) and 9 females (8.11%) were G6PD deficient. These were similar to the results reported by Pramuji *et al* in 1995 for the people around Palembang. Since the G6PD gene is located on the X chromosome, this is a peculiar result thus further studies need to be done. In cooperation with Harvard University, Sumantri *et al* in 1995 described 14% as carriers. Molecular analysis among these 16 Javanese males showed the following mutations - nt563 (C->T) in 5 cases, nt1376 (G->T) in 3 cases, nt487 (G->A) in 2 cases, nt1311 (C->T) in 1 case with the remaining variants unknown.

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) is a cytoplasmic enzyme whose main metabolic role is the production of NADPH in the monophosphate pathway as the defense against oxidizing agents. Clinical symptoms of G6PD deficiency are always associated with hemolysis induced by viruses, drugs, and foods such as fava beans. As a malaria endemic area, Indonesia is estimated to be one of the most prevalent countries for Glucose-6-phosphate dehydrogenase (G6PD) deficiency carriers (Ganczakowski *et al*, 1995). Even if there are no extensive studies yet, it is estimated that around 2-6% of the general population (male and female) were carriers. This disease is X-linked and the severity depends on the location of the mutation. Sex is also one determinant with greater severity in males.

Gene affected individuals are asymptomatic and non anemic except when hemolysis occurs induced by infection, metabolic disturbance or exposure to drugs or chemicals. Indonesia with 225 million inhabitants scattered in 4 big and 400 small islands, has only a few small scale studies that covered less than 0.1% of the population. Due to the rarity of victims and the limited resources, investigation of the G6PD variant is always waived from the health research program by the health authority.

In Thailand, Tanpaichitr (1999) mentioned that the most prevalent variants are G6PD Mahidol (163 Gly -> Ser), Canton (1376 G ->T) and Bangkok Noy (1502 T -> G). It is generally believed that neonatal hyperbilirubinemia caused by G6PD deficiency is an important clinical consequence in which the risk of kernicterus is increasing. Among 600 newborn babies evaluated within 5 months in one of the Private Hospitals in Yogyakarta, only three of the 34 newborns with jaundice had low G6PD blood levels. In these cases, the G6PD blood levels were 95 to 110 pp/1000 erythrocytes. The local normal level is 125 pp/1000 erythrocytes.

The strategy to decrease mortality and morbidity is mass screening of G6PD deficiency during the first week of life to prevent kernicterus (Brown and Boon, 1968). Follow-up is important for affected individuals to guarantee early effective management to prevent acute hemolytic anemia in children which often leads to death in places where health facilities are limited.

METHODS AND RESULTS

The Formazan Ring Method which screens the activity of the G6PD enzyme (Purnomo *et al*, 1998) has been used to study 145 male newborn infants in Yogyakarta and its surrounding areas. It revealed that 6.2% had moderate, 1.6% had low and the rest had normal G6PD activity.

In Yogyakarta, 111 newborn blood samples were analyzed for G6PD content by UV methods and no deficient levels were found (Tasmini *et al*, 1995). In the western part of Indonesia, in Sumatra island, individuals of Batak descent were studied using the Sigma Kit (Sofro *et al*, 1994). The G6PD content of 134 samples was determined and 10 samples from males (43.5%) and 9 from females (8.1%) were deficient. A similar study was performed in Palembang (1000km south of Medan, Sumatra) with the same conclusions.

Since the G6PD gene is X-linked, gene analysis is important to clarify the variants and/or one or both affected chromosomes of the individual. This is necessary for genetic counseling and marriage consultation. In Java island, gene analysis was conducted on 16 DNA samples from G6PD deficient cases of Semarang, a city with many individuals of Chinese descent (Soemantri *et al*, 1995). Five cases of nt563 (C->T) Mediterranean variant were reported along with 1 case of nt311 (C->T), 3 cases of nt1376 (G->T) Canton, and 2 cases of nt487 (G->A) Mahidol. Exons 6, 11, and 12 were analyzed in seven DNA samples of G6PD deficiency cases from Yogyakarta using the MPTP method (Shirakawa *et al*, 1997) to detect 6 South Asian G6PD deficient variants (Mahidol, Taiwan Hakka, Mediterranean, Union, Canton and Kaiping). The report did not show any significant results (Purnomo *et al*, 1999).

DISCUSSION

In Indonesia, screening programs and monitoring are still big problems from the point of view of human resources, facilities and transportation. Awareness for screening at the molecular level is still in theory, and support from health authorities is always minimal it being a low priority.

Indonesia is a new nation. With its complexity of ethnic groups, gene anomaly is an interesting aspect of disease to study because of the possibility that new genetic variants are always expected to appear aside from those in previous publications. Peculiar problems in such diseases could be disclosed in a case as a new mutation or a new variant. Screening using the MPTP method showed that the 6 most prevalent variants in exons 6, 11 and 12 were detected in neighbouring countries. This was not shown in the 7 G6PD deficient samples from Jakarta (Purnomo *et al*, 1998). These are probably different variants in different exon locations. The type of mutations may be different from those previously reported in Thailand (Kurdi H *et al*, 1990, Panich *et al*, 1980) and China (Saha *et al*, 1994). Investigation at the molecular level is needed to clarify the presence of the disorder.

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