Clin. Lab. 2018;64:XXX-XXX

SHORT COMMUNICATION

Prevalence of Glucose-6-Phosphate Dehydrogenase Deficiency in Sichuan, China

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SUMMARY

Background: **Our goals were to screen newborns and characterize the occurrence of glucose-6-phosphate dehydrogenase (G6PD) deficiency in southwestern China. Meanwhile, we would like to analyze the factors that might affect the results of neonatal dried blood spots for glucose-6-phosphate dehydrogenase screening test, to improve the clinical quality control level, effectively reduce the external factors in the process of detection.**
Methods: **This study involved an evaluation of G6PD data for 20,644 newborns from a universal newborn screening program. Heel prick blood specimens were collected around 72 hours after birth and were dried on filter papers. For G6PD deficiency the fluorescent spot test was employed. We studied the association between incidence of G6PD deficiency and influence factors.**
Results: **This study involved an evaluation of G6PD data for 20,644 neonatal heel prick blood samples from 10,984 males and 9,660 females. There were 503 positive results for G6PD deficiency (299 males and 204 females), and the G6PD deficiency-positive rate was estimated to be around 2.4%. The gender-specific prevalence for males was 2.7%, and for females 2.1%. Multiple factors may influence the result of the G6PD test, such as season, temperature, and specimen of indwelling time.**
Conclusions: **This study analyzed the prevalence of G6PD deficiency in Sichuan, China. Accelerating the speed of sample delivery and ensuring availability of screening results can aid the screening and diagnosis.**
(Clin. Lab. 2018;64:xx-xx. DOI: 10.7754/Clin.Lab.2017.170330)

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Short Communication accepted October 30, 2017

KEY WORDS

neonatal screening, glucose-6-phosphate dehydrogenase, deficiency, influence factor

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency, the most common human enzymopathy and most commonly found in males due to X-linked heritability, is an important public health problem and affects some 400 million people worldwide [1]. In regions of the world such as tropical Africa the prevalence of G6PD deficiency ranges from 15 - 26% [2]. The highest prevalence in the world is in Africa, Southern Europe, the Middle East, Southeast Asia, Mediterranean countries, and the central and southern Pacific Islands. The public health burden of this condition is significant. However,

due to global migration, currently, the disease is widely distributed around the world, having significant differences in different areas between different ethnic groups [3]. China is one of the prevalent places with G6PD deficiency. The most common areas are reported in Sichuan, Guangdong, Guangxi, and Yunnan provinces in China. Then neonatal screening was extended to all provinces in China over the next two decades [4]. G6PD deficiency will cause intravascular hemolysis, induced by high neonatal bilirubin levels, and hemolytic anemia during the growth of children. The most common clinical manifestation in the neonatal period is neonatal jaundice, which is accompanied by hyperbilirubinemia and puts infants at risk for kernicterus within the first few days of life [5]. Kernicterus can lead to hearing deficits, behavior problems, and permanent neurologic damage [6].

Screening of newborns for G6PD deficiency has emerged as an essential component of neonatal care in developed countries. Because the disease is common in southwestern China and rarely reported in Sichuan, the screening of G6PD deficiency has been added to the newborn screening in our city to effectively prevent the disease.

However, the newborn screening ethics issues are also increasing. The primary benefit and goal of screening for G6PD deficiency is the accurate identification of the few babies from a normal population of newborn babies or from those who seem to have the symptoms of hyperbilirubinaemia. Some health professionals believe that it is unethical to conduct a screening programme until adequate facilities and skilled personnel are available to deal with all the consequences of the screening programme [7,8]. In the absence of screening, G6PD deficiency is unlikely to be detected until the parents or caregivers observe a child's sclera present mild yellow color and urine has the color such as black tea, or even like soy sauce. Early detection and prevention of these conditions is a key strategy, since timely intervention can lead to significant reductions of morbidity, mortality and associated disabilities in affected infants [9]. Consequently, we believe that early detection of G6PD should be encouraged in developing countries, even where intervention services are limited but evolving. In China, newborn screening of G6PD mainly through the filter paper method of dried blood test is an important means of prevention and treatment of hyperbilirubinemia for newborns. In our research, we employed the fluorescent spot test to determine the prevalence of G6PD deficiency in Sichuan screened during January 2015 to June 2016. We assessed the prevalence of G6PD deficiency and the factors that influence test results in relation to demographic characteristics, seasons, temperature, specimen transportation and preservation time.

MATERIALS AND METHODS

Materials

A total of 20,644 heel blood specimens (10,984 males and 9,660 females) were collected from West China Second University Hospital from January 1, 2015 to June 30, 2016, including normal newborns and those who were diagnosed with probable G6PD deficiency. Seventy-two hours after babies are born with sufficient lactation and after informing the parents about the process in detail, we obtain heel blood and spot on filter paper (S&S903) maintaining a diameter greater than 8 mm and penetration to the back of filter paper. After the spots are naturally air-dried they are placed in a plastic bag at 2 - 8°C to preserve the test (Perkin Elmer G-6-PD kit).

Methods

Hematological data were analyzed in dried blood spots by fluorescent spot test. The determination criterion: positive ≤ 2.6 g/Hb, normal > 2.6 g/Hb, recommended by kit instructions and validated in our laboratory.

Statistical analysis

SPSS 22.0 was used for statistical analysis. Data were presented as means ± standard deviation. All experiments were performed in triplicate, unless otherwise stated. Data were analyzed with chi-square test and Student's *t*-test or *F*-test where appropriate. Significance was accepted at $p < 0.05$ by using adjustment to unequal groups of data.

RESULTS

A total of 20,644 children (10,984 males and 9,660 females) were screened for G6PD deficiency. Children ranged in age from 0 months to 3 years. The overall prevalence of G6PD deficiency was 2.4% in all children. In males, the prevalence was 2.7% and in females it was 2.1%. The odds for male and female children were not significantly different.

The relationship of incidence of G6PD deficiency with gender

Neonatal screening for G6PD deficiency for 20,644 cases (10,984 boys and 9,660 girls) showed positive results in 503 cases. The G6PD deficient rate was 2.4% in total. The incidence rate of neonatal G6PD deficiency in boys was 2.7%, which was higher than that in girls ($p < 0.05$) (Table 1).

The relationship of incidence of G6PD deficiency with age

We investigated the relationship between age group and G6PD deficiency. The result indicated that the incidence of G6PD deficiency decreased with age. This classification could be useful for patients and clinicians to pay more attention to infants (Table 2).

Table 1. The relationship of incidence of G6PD deficiency with gender.

Gender	Total screening	G6PD deficiency	Incidence (%)	χ^2	p-value
Males	10,984	299	2.7	8.054	< 0.05
Females	9,660	204	2.1		
Total	20,644	503	2.4		

Table 2. The relationship of incidence of G6PD deficiency with age.

Age	Total screening	G6PD deficiency	Incidence (%)	χ^2	p-value
0 - 28 days	18,470	481	2.6	17.49	< 0.05
29 days - 3 months	310	6	1.9		
3 months - 1 year	1,046	1	0.1		
1 year - 3 years	818	15	1.8		
Total	20,644	503	2.4		

Table 3. The influence factors of dried blood test results (n = 13,376, U/gHb).

Influence factors		n	Level of G6PD ($\overline{\chi} \pm s$)	*F*- or *t*-test	p-value
Season	spring and summer	8,755	4.39 ± 0.20	3.531	< 0.05
	autumn and winter	4,621	5.18 ± 0.10		
Gender	males	7,709	5.05 ± 0.10	0.7618	> 0.05
	females	5,667	4.95 ± 0.10		
Temperature	2 - 8°C	20	4.56 ± 0.14	4.505	< 0.05
	room temperature	20	4.34 ± 0.29		
Specimens of indwelling time (d)	1	20	5.42 ± 0.24	3.742	< 0.05
	2	20	4.92 ± 0.40		
	3	20	4.76 ± 0.14		
	4	20	4.26 ± 0.12		

The influence factors of dried blood test results

The level of G6PD in spring and summer was significantly lower than autumn and winter, while there is no difference between females and males. When the specimens are preserved in 2 - 8°C, the detection value is higher than if they are preserved in room temperature, and the difference was significant. Furthermore, the test results of G6PD gradually decreased with the specimens of indwelling time extension (Table 3).

DISCUSSION

In order to ensure the healthy growth of children, it is necessary to carry out the newborn screening. The general principles governing medical ethics applied to how newborn screening should be conducted consist of autonomy (the right to choose), beneficence (obligations to provide benefits and to balance benefits against risks), non-maleficence (obligation to avoid causing harm), and justice (obligations of being fair and equitable in the distribution of benefits and risks) [10]. If the risk or cost of screening is greater than the beneficence or influence, the screening is not feasible. When

deciding whether to adopt common compulsory testing, we should consider the benefits and burdens that doing screening will bring to the screening, negative and positive. Due to a lack of clear follow-up intervention and treatment measures for confirmed cases, some screening does not bring actual benefits to children, which only makes the parents worry and lose confidence. Such screening should be considered thoroughly before implementation.

Implementation of neonatal screening for G6PD deficiency should solve the following problems, including specimen collection, sending and screening specimen as early as possible, reporting the screening results as soon as possible, and giving relevant information of G6PD deficiency to avoid the occurrence of newborn hyperbilirubinemia and hemolytic anemia as far as possible. Carrying out the screening of G6PD and controlling inducements will contribute to G6PD deficient individuals obtaining timely diagnosis and reasonable treatment, which will greatly reduce incidence of the disease. G6PD deficiency is best screened by both quantitative and genotype screening methods. The mechanism of deficiency is associated with mutations in the G6PD gene. Although the newborn G6PD screening started later than in other cities in China, our survey results timely revealed the condition of G6PD deficiency in Sichuan province. In the future, efforts will be committed to continued education of providers about the screening program, continued improvement of resources for family education, and ensuring conveyance of results of G6PD testing.

CONCLUSION

This study describes the relationship of incidence of G6PD deficiency with a variety of influence factors and the related ethics of neonatal screening programs. Taken together, these results may provide insightful answers to the incidence of G6PD deficiency in our province. It is important to continue the ongoing implementation and expansion efforts so that these children can attain the same health status as children in more developed parts of the world. Thus, the government should attach great importance to the promotion of this screening to improve the quality of life for the population in our country.

Declaration of Interest:

We declare that we have no conflict of interest.

References:

1. Nkhoma ET, Poole C, Vannappagari V, Hall SA, Beutler E. The global prevalence of glucose-6-phosphate dehydrogenase deficiency: a systematic review and meta-analysis. Blood Cells Mol Dis 2009;42(3):267-78 (PMID: 19233695).
2. Williams O, Gbadero D, Edowhorhu G, Brearley A, Slusher T, Lund TC. Glucose-6-Phosphate Dehydrogenase Deficiency in Nigerian Children. PLoS One 2013;8(7):e68800 (PMID: 23874768). PMCID:PMC3709898.DOI:10.1371/journal.pone.0068800.
3. Beutler E. G6PD deficiency. Blood 1994;84(11):3613-36 (PMID: 7949118).
4. Gu XF, Chen RG. Current status of neonatal screening in China. J Med Screen 1999;6(4):186-7 (PMID: 10693062).
5. Watchko JF. Identification of neonates at risk for hazardous hyperbilirubinemia: emerging clinical insights. Pediatr Clin N Am 2009;56(3):671-87 (PMID: 19501698).
6. Shapiro SM, Bhutani VK, Johnson L. Hyperbilirubinemia and kernicterus. Clin Perinatol 2006;33(2):387-410 (PMID: 16765731).
7. Gilbert R, Logan S, Moyer VA, Elliott EJ. Assessing diagnostic and screening tests: Part 1. West J Med 2001;174(6):405-9 (PMID: 11381009).
8. Paradise JL. Universal newborn hearing screening: should we leap before we look? Pediatrics 1999;103(3):670-2 (PMID: 10049975).
9. American Academy of Pediatrics. Serving the family from birth to the medical home. Newborn screening: a blueprint for the future - a call for a national agenda on state newborn screening programs. Pediatrics 2000;106(2 Pt 2):389-422 (PMID: 10947682).
10. Beauchamp TL. Methods and principles in biomedical ethics. J Med Ethics 2003;29(5):269-74 (PMID: 14519835).