

A study of glucose-6-phosphate dehydrogenase deficiency in neonatal hyperbilirubinemia

Harshid Patel¹, Nikunj Patel², Amit Maniyar³, Karan Gandhi⁴, Rupali Patil⁵

¹Department of Pathology, GMERS Medical College, Dharpur-Patan, North Gujarat, India.

²Department of Bio-chemistry, GMERS Medical College, Dharpur-Patan, North Gujarat, India.

³Department of Pathology, C. U. Shah Medical College, Surendranagar, Gujarat, India.

⁴Department of Pathology, Accurate Path. Lab., Himmatnagar, Gujarat, India.

⁵Department of Pathology, B. J. Medical College, Ahmedabad, Gujarat, India.

Correspondence to: Harshid L Patel, E-mail: drhlp1975@gmail.com

Received November 20, 2014. Accepted December 15, 2014

Abstract

Background: Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme essential for basic cellular functions, including protection of red cell proteins from oxidative damage. G6PD deficiency is the most common red cell enzyme abnormality associated with hemolysis as well as with neonatal jaundice, kernicterus, and even death. It plays a protective role against malaria. It is a genetically inherited sex-linked abnormality.

Objectives: To determine the age, sex, and different community-wise incidence of G6PD deficiency in neonatal subjects having neonatal hyperbilirubinemia.

Materials and Methods: This study was carried out among 170 neonates at Biochemistry Department of B.J. Medical College & Civil Hospital, Ahmedabad, Gujarat, India, between August 2007 and July 2009.

Results: Of 170 neonates, 123 were males and 47 were females, and 18 neonates showed deficiency of G6PD in red cells. Parsi community had highest incidence of G6PD enzyme deficiency. Muslim community had higher incidence than Hindu community because of consanguineous marriages. Of total 18 G6PD enzyme-deficient subjects, 11 were early neonates and 7 were late neonates. Of these 11 G6PD enzyme-deficient early neonates, 5 were 6-day old. Highest incident was found on 2-day-old neonates.

Conclusion: The G6PD-deficient neonates are prone to a greater incidence of neonatal jaundice. Methylene blue reduction test is useful screening procedure, so the quantitative enzyme assay must be used for a definitive diagnosis of G6PD deficiency.

KEY WORDS: Enzyme, glucose-6-phosphate dehydrogenase, neonatal hyperbilirubinemia


Introduction

Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme essential for basic cellular functions, including protection of red cell proteins from oxidative damage.

The G6PD deficiency increases hemoglobin vulnerability to oxidative damage, leading to hemoglobin instability and precipitation of Heinz bodies.^[1]

G6PD deficiency is the most common red cell enzyme abnormality associated with hemolysis. It is also known to be associated with neonatal jaundice, kernicterus, and even death. The marked elevation of bilirubin levels that sometimes occurs in the neonatal period raises the risk of kernicterus. Neonatal hyperbilirubinemia often arises in association with Gilbert's syndrome.^[2,3] It affects over 400 million people worldwide.^[4]

G6PD deficiency occurs with increased frequency throughout Africa, Asia, the Mediterranean, and the Middle East. In the United States, black males are most commonly affected, with a prevalence of approximately 10%.^[5] The global distribution and health burden of G6PD deficiency has

| Access this article online | |
|--|---|
| Website: http://www.ijmsph.com | Quick Response Code:  |
| DOI: 10.5455/ijmsph.2015.20112014125 | |

International Journal of Medical Science and Public Health Online 2015. © 2015 Harshid L Patel. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material for any purpose, even commercially, provided the original work is properly cited and states its license.

been reviewed by the World Health Organization (WHO).^[4] About 7.5% of the world's population carries a gene for G6PD deficiency, the proportion ranging from a maximum of 35% in parts of Africa to 0.1% in Japan and parts of Europe. The distribution of populations with high frequency of G6PD deficiency geographically overlaps closely with the prevalence of malaria, suggesting that G6PD deficiency may play a protective role against malaria.^[6]

G6PD is a housekeeping gene expressed in all the tissues. Due to its extreme importance in red blood cells, mutants showing 100% deficiency of the G6PD enzyme will be incompatible with life and are thus not reported. Indeed gross deletion, nonsense mutations, frame-shift mutations, and splicing defects are not reported for this gene.^[7,8] Using biochemical methods, 442 variants of G6PD enzyme have been identified. Of these, 299 were characterized by methods agreed on by the WHO.^[4] The G6PD variants have been divided into five classes by the WHO according to their activity in the red cell. G6PD deficiency is genetically inherited sex-linked abnormality. The gene encoding G6PD located on the X-chromosome, (Xq28), is over 20 Kb in length and contains 13 exons.^[9]

Being sex-linked condition, the prevalence of G6PD deficiency in any given population is determined by the number of deficient males.^[10] However, deficient females are also at risk of hemolysis and jaundice.

Materials and Methods

In this study, total 170 neonates having hyperbilirubinemia were selected. Informed consent was obtained from all subjects. Approval from ethics committee of the institution was taken before commencing the study. After taking consent from each patient, 5 ml blood was withdrawn from each of the neonate by aseptic method in K3 EDTA vacutainer. The duration of this study was between August 2007 and July 2009 at B.J. Medical College & Civil Hospital, Ahmedabad, Gujarat, India.

All these samples were checked for G6PD activity by methemoglobin reduction test. After completing these procedures, all samples were interpreted as G6PD present, which show clear red color, and as G6PD deficient, which show brown color. All the samples showing G6PD deficiency were retested by repeating the same method.

Results

In this study, total 170 neonates having hyperbilirubinemia were selected at B.J. Medical College & Civil Hospital during period of 2 years between August 2007 and July 2009. Of 170 neonates, 123 (72.4%) were males and 47 (27.6%) were females. Of 170 neonates, 18 (10.6%) neonates showed deficiency of G6PD in red cells. Total incidence of G6PD enzyme deficiency was found to be 10.6%. Male neonates showed having higher incidence of 12.2% compared to females having an incidence of 6.4%.

Among these 170 subjects, 118 (69.4%) belonged to Hindu community and 28 (16.5%) to Muslim community. Among these 18 G6PD enzyme-deficient subjects, 11 (61.1%) were of Hindu and 4 (22.2%) were of Muslim communities. Among all these communities, Parsi community had highest incidence (33.3%) of G6PD enzyme deficiency followed by Sindhi community (16.7%), mostly because of smaller sample size. Muslim community had higher incidence (14.3%) than Hindu (9.3%) community because of consanguineous marriages. No deficient neonates were found among Rajput, Marathi, and Sikh communities. Overall incidence was found to be higher than general in neonates of Parsi, Sindhi, and Muslim communities, whereas it was lower than general in neonates belonging to Marwadi and Hindu communities. Sex-wise distribution showed highest incidence rate of 50.0% among Parsi male neonates, followed by Muslim and Sindhi neonates having same incidence rate of 16.7%, which is higher than general incidence rate (6.4%).

Among total 170 subjects, 39 (22.9%) were early neonates (aged up to 7 days) and 131 (77.1%) were late neonates (aged 8 to 28 days). Among these 39 early neonates, 17 (43.6%) were 6-day old, 9 (23.1%) were 5-day old, and 6 (15.4%) were 4-day old. Among total 18 G6PD enzyme-deficient subjects, 11 (61.1%) were early neonates and 7 (38.9%) were late neonates. Among these 11 G6PD enzyme-deficient early neonates, 5 (45.5%) were 6-day old, 3 (27.3%) were 5-day old, and 2 (18.2%) were 2-day old.

Discussion

In this study, total incidence of G6PD enzyme deficiency is 10.6%. Male neonates were found to have higher incidence of 12.2% compared to females having an incidence of 6.4%. Among these 18 G6PD enzyme-deficient subjects, 61.1% were from Hindu and 22.2% were from Muslim communities. Among total 18 G6PD enzyme-deficient subjects, 61.1% were early neonates and 38.9% were late neonates. Among these 11 G6PD enzyme-deficient early neonates, 45.5% were 6-day old, 27.3% were 5-day old, and 18.2% were 2-day old.

In the study of Gupte *et al.*^[11], of total 1644 subjects, 359 (21.8%) were having G6PD enzyme deficiency. In the study of Pao *et al.*^[12], of total 2479 subjects, 50 (2.0%) were having G6PD enzyme deficiency. In the study of Kuruvilla *et al.*^[13], of total 212 subjects, 25 (11.8%) were having G6PD enzyme deficiency. In this study, total incidence of G6PD enzyme deficiency was found to be 10.6%, which is closely similar with the findings of the study by Kuruvilla *et al.*,^[13] higher than the study by Pao *et al.*,^[12] and lower than the study by Gupte *et al.*^[11]

G6PD is an X-linked condition and males are therefore more commonly and more severely affected than females. Neonatal jaundice is the most common clinical presentation. So in a population with a high prevalence rate, early detection of G6PD enzyme deficiency by neonatal screening is desirable to take appropriate measures to prevent the complications of hemolysis and jaundice.

Conclusion

The G6PD-deficient neonates are prone to a greater incidence of neonatal jaundice. Methylene blue reduction test is useful screening procedure, so the quantitative enzyme assay must be used for a definitive diagnosis of G6PD deficiency. Highest incidence of G6PD deficiency was found in Parsi community because of smaller sample size followed by Sindhi, Muslim, and Marwadi communities. No deficient neonate was found among Rajput, Marathi, and Sikh communities. Sex-wise distribution among all different communities showed highest incidence rate among male neonates than among their female counterparts. Highest incidence rate of G6PD deficiency was found to be among 2-day-old neonates.

In a population with a high prevalence rate, early detection of G6PD enzyme deficiency by neonatal screening is desirable to take appropriate measures to prevent the complications of hemolysis and jaundice.

Acknowledgments

We are thankful to respected parents of all 170 neonates and all technical staff members of Biochemistry Department, BJ Medical College & Civil Hospital, Ahmedabad, Gujarat, India, for their valuable work in our study.

References

- Ronquist G, Theodorsson E. Inherited, non-spherocytic haemolysis due to deficiency of glucose-6-phosphate dehydrogenase. *Scand J Clin Lab Invest* 2007;67:105–11.
- McPherson RA, Pincus MR. *Henry's Clinical Diagnosis and Management by Laboratory Methods*, 21st edn. Saunders Elsevier, 2008. p. 533.
- Kaplan M, Hammerman C. Glucose-6-phosphate dehydrogenase deficiency: a potential source of severe neonatal hyperbilirubinaemia and kernicterus. *Semin Neonatol* 2002;7:121–8.
- WHO Working Group. Glucose-6-phosphate dehydrogenase deficiency. *Bull World Health Organ* 1989;67:601–11.
- Frank JE. Diagnosis and management of G6PD Deficiency. *Am Fam Physician* 2005;72(7):1277–82.
- Ruwende C, Khoo SC, Snow RW, Yates SN, Kwiatkowski D, Gupta S, et al. Natural selection of hemi- and heterozygotes for G6PD deficiency in Africa by resistance to severe malaria. *Nature* 1995;376:246–9.
- Beutler E, Kuhl W. The NT 1311 polymorphism of G6PD: G6PD Mediterranean mutation may have originated independently in Europe and Asia. *Am J Hum Genet* 1990;47:1008–12.
- Mehta A. Glucose-6-phosphate dehydrogenase deficiency. *Best Pract Res Clin Haematol* 2000;13:21–38.
- Takizawa T, Huang IY, Ikuta T, Yoshida A. Human glucose-6-phosphate dehydrogenase: primary structure and cDNA cloning. *Proc Natl Acad Sci USA* 1986;83:4157–61.
- Mallouh AA, Imseeh G, Abu-Osba YK, Hamdan JA. Screening for glucose-6-phosphate dehydrogenase deficiency can prevent severe neonatal jaundice. *Ann Trop Pediatr* 1992;12:391–5.
- Gupte SC, Patel PU, Ranat JM. G6PD deficiency in Vataliya Prajapati community settled in Surat. *Indian J Med Sci* 2005;59(2):51–6.
- Pao M, Kulkarni A, Gupta V, Kaul S, Balan S. Neonatal screening for glucose-6-phosphate dehydrogenase deficiency. *Indian J Pediatr* 2005;72(10):835–7.
- Kuruvilla KA, Sukumar ST, Jana AK. Glucose-6-phosphate dehydrogenase deficiency in neonatal hyperbilirubinemia in a south Indian referral hospital. *Indian Pediatr* 1998;35:52–5.

How to cite this article: Patel H, Patel N, Maniyar A, Gandhi K, Patil R. A study of glucose-6-phosphate dehydrogenase deficiency in neonatal hyperbilirubinemia. *Int J Med Sci Public Health* 2015;4:621-623

Source of Support: Nil, **Conflict of Interest:** None declared.