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Pediatric Provider Insight into Newborn Screening for G6PD Deficiency

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Abstract

Objective—G6PD deficiency is a major contributor to neonatal hyperbilirubinemia, yet newborn screening for this disorder in the United States is not standard practice. We surveyed pediatric provider's response to a novel newborn G6PD screening program successfully implemented in a US urban women's hospital newborn nursery in 2007.

Study Design—An electronic survey was distributed to 472 pediatric providers addressing extent to which they were influenced by the screening program.

Results—Ninety-two (20%) of providers responded, of whom 74 (80%) had taken care of G6PD deficient patients diagnosed by the screening program. A majority found the diagnosis helpful for patient management and influential in their management. Most common changes in management included more counseling on jaundice and follow up and avoidance of hemolytic crisis triggers.

Conclusions—General pediatric providers support newborn G6PD screening and appreciate the current program. Knowing the G6PD deficiency status of newborns informed and influenced pediatric providers' care.

Keywords

hyperbilirubinemia; neonatal; screening; glucose-6-phosphate deficiency; management

Introduction

Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency, the most common human enzyme defect, affects more than an estimated 400 million people worldwide, most commonly males due to X-linked heritability.[1] While the majority of G6PD deficient patients remain asymptomatic as children and adults, these patients have an increased risk of significant

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neonatal hyperbilirubinemia, and thus, kernicterus, due to hemolytic crisis or baseline increase in red blood cell breakdown with concomitant diminished bilirubin conjugation.[2-4] The American Academy of Pediatrics (AAP) recognizes G6PD deficiency as a major risk factor for the development of severe hyperbilirubinemia, and recommends that treatments for hyperbilirubinemia, such as phototherapy and exchange transfusion, occur at lower total bilirubin levels in infants with G6PD deficiency than in those without.[5] G6PD deficiency is also overrepresented as a cause of kernicterus.[5-7] In a US registry, G6PD deficiency accounted for 20.8% of reported kernicterus cases, the majority of which are in black neonates.[7,8]

Screening for G6PD deficiency in newborns may contribute to early identification of infants at risk for hyperbilirubinemia. Currently, G6PD screening in the US is not routinely performed and the AAP only recommends testing in jaundiced newborns receiving phototherapy with family history, ethnicity or geographic origin suggestive of G6PD deficiency or for infants with poor response to phototherapy.[5,9] There is currently no well-established consensus on the need or type of G6PD screening within the neonatal period,[9,10] although the World Health Organization recommends G6PD screening via the fluorescent spot test among populations where 3-5% of males are affected.[9,11] In the US, Washington DC and Pennsylvania have included G6PD DNA screening in their state newborn screening programs,[12] but the results may take weeks to be returned, limiting their usefulness during the high-risk early neonatal period.[9]

In 2007, we established a novel G6PD neonatal screening program at MacDonald Women's Hospital in Cleveland, OH, where 50-60% of infants are born to black mothers, by screening at-risk males, as determined by maternal questionnaire, with umbilical cord blood fluorescent spot testing.[13] The screening program determined that 11.1% of screened male newborns were G6PD deficient. Nearly all (98%) test results were reported within 48 hours, allowing for family counseling and care provider acknowledgement of risk factors for the development of hyperbilirubinemia prior to discharge.[13] The implementation of the program included education of pediatric providers and nursing staff and the development of a Patient Information hand-out to give to parents and aid in family counseling about the disorder. The screening program has been in existence for several years, but its impact on how general pediatric providers care for patients with G6PD deficiency and their attitudes about the program had not been examined.

Subjects and Methods

The study was approved by the University Hospitals Institutional Review Board. Two groups of pediatric providers were surveyed: (1) those that provide care to MacDonald Hospital newborns in both the MacDonald Hospital Newborn Nursery as well as in an outpatient setting and (2) those that provide only outpatient care to MacDonald Hospital newborns. Providers included general pediatric attending physicians and residents, family medicine attending physicians, and nurse practitioners.

A 9-item survey was developed. Survey questions assessed site of their care of infants born at MacDonald, involvement in care of G6PD deficient patients diagnosed by the program,

family counseling, and influence of G6PD diagnosis on management. Surveys were distributed to pediatric providers via email. Three reminder emails were sent out every two weeks following initial distribution. Study data were collected and managed using REDCap electronic data capture tools hosted at University Hospitals. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies. Survey responses were described using frequencies and proportions. JMP 9.0 Statistical was used for descriptive analyses (Software Institute Inc., Cary, North Carolina, USA).

Results

Of the 472 pediatric providers, 92 (20%) responded. Among those who responded, 74 (80%) had cared for patients with G6PD deficiency. Forty-six (62%) of these individuals saw G6PD patients in the inpatient and outpatient setting, while 30 (41%) provided care for G6PD patients only in the outpatient setting.

A large majority (n = 46, 93%) of the inpatient and outpatient providers found the G6PD diagnosis helpful in management, and 36 (78%) actually changed their practice because of the diagnosis. Specific changes made to management are listed in Table 1. Twenty-eight (93%) of outpatient only providers found the G6PD diagnosis helpful in management, with 24 (80%) changing their practice because of it. Table 2 displays changes made to management of G6PD patients as outpatients-only.

Both sets of providers were asked how they felt parents perceived the diagnosis. The majority felt that parents seem to understand that G6PD deficiency is a risk of neonatal hyperbilirubinemia but is unlikely to cause significant problems in the future (n = 50, 74%). Thirteen percent (n = 9) of providers felt the diagnosis seemed to increase parental worry about their baby and his future and another thirteen percent felt that parents seemed to have no understanding of or concern about G6PD diagnosis.

Several respondents provided open-ended responses when asked if there was anything else they would like to share about the G6PD screening program at MacDonald’s Hospital for Women. Some comments offered quality improvement suggestions for the screening program. Others offered support of the program and reinforcement of its utility (Table 3).

Discussion

This project sought to examine the impact a recently implemented G6PD screening program of high-risk males has had upon general pediatric care providers at a tertiary care hospital in Cleveland, OH. Initial examinations of the screening program identified a low cost, rapid, and effective screening tool which can be used as a model for general pediatricians in identifying another risk factor for neonatal hyperbilirubinemia, G6PD deficiency, specifically in high-risk infants often seen in outpatient follow up appointments.[13] The present study illustrates that general pediatric providers support G6PD screening, like the current screening program and have changed their management when knowing of the diagnosis of G6PD deficiency. Furthermore, providers perceive that the diagnosis of G6PD deficiency is well-accepted and understood by most parents.

Some of the most convincing evidence in support of newborn screening comes from areas of high prevalence, such as Asian, African, Mediterranean and Middle Eastern countries. Reports have shown that countries like Greece, Philippines, Israel, and India successfully utilize newborn diagnosis of G6PD deficiency to identify at-risk infants and prevent complications,[14-18] while studies in Singapore, Saudi Arabia, and Sardinia reported decreased rates of kenicterus,[19-20] and favism.[21] In Singapore, in particular, newborn screening essentially eradicated kernicterus secondary to G6PD deficiency, with no newborn deaths attributed to this cause at least two decades following screening implementation.[19]

Discussions of universal testing for G6PD deficiency continue to grow within the United States,[5] and universal screening is currently supported by many pediatricians.[5,9,22-23] While certain areas of the United States may be considered at low risk for G6PD deficiency, communities with large at-risk populations are at an increased threat and may benefit greatly from testing. Migration and intermarriage have further contributed to making G6PD deficiency a more global problem than in the past.[1,2,7,9,24] This study, implemented in an area with high number of at risk infants supports that the diagnosis is beneficial to health care providers and understandable to patients' families.

This study has several limitations. Similar to all survey studies, it is limited by the response rate. A wide number of pediatric providers were surveyed, some of whom are less connected with academic medicine and some who may not have any exposure to the screening program or cared for in infant with G6PD deficiency. These providers would be less likely to respond. List serves were utilized which contained several dozen unreliable email addresses. In addition, this is a single-center survey based upon the unique screening program. Finally, there is no validated questionnaire for our study and it was therefore constructed to maximize understanding and response rate.

In the future, efforts will be directed towards continued education of providers about G6PD deficiency and the screening program, continued improvement of the program and resources for family education, and ensuring conveyance of results of G6PD testing to outpatient providers. Further evaluation of the screening program, such as cost effectiveness and readmission and complication rates, can provide more insight into effectiveness of the program. Finally, it would be valuable to learn the families' perspective and understanding of the G6PD diagnosis so as to better provide counseling and prevent severe neonatal hyperbilirubinemia due to G6PD deficiency and future complications. Family counseling provides a critical avenue in early identification of problems related to jaundice.[23]

In conclusion, this initial evaluation of our institution's G6PD deficiency screening program strongly supports its usefulness to providers in providing excellent care for newborns. Dangerous complications of neonatal hyperbilirubinemia are preventable and evidence supports the use of newborn G6PD screening programs in reducing such complications as hospital readmissions and kenicterus.

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References

1. Cappellini MD, Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. Lancet. 2008; 5(371): 64–74. [PubMed: 18177777]
2. Beutler E. Glucose-6-phosphate dehydrogenase deficiency: a historical perspective. Blood. 2008; 111:16–24. [PubMed: 18156501]
3. Kaplan M, Hammerman C, Renbaum P, Levy-Lahad E, Vreman HJ, Stevenson DK. Differing pathogenesis of perinatal bilirubinemia in glucose-6-phosphate dehydrogenase-deficient versus-normal neonates. Pediatr Res. 2001; 50:532–7. [PubMed: 11568299]
4. Sgro M, Campbell D, Shah V. Incidence and causes of severe neonatal hyperbilirubinemia in Canada. CMAJ. 2006; 175:587–90. [PubMed: 16966660]
5. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Clinical practice guideline; management of hyperbilirubinemia in the newborn Infant 35 or more weeks of gestation. Pediatrics. 2004; 114:297–316. [PubMed: 15231951]
6. Watchko JF. Identification of Neonates at Risk for Hazardous Hyperbilirubinemia: Emerging Clinical Insights. Pediatr Clin N Am. 2009; 56:671–87.
7. Bhutani VK, Johnson LH, Maisels MJ, Newman TB, Phibbs C, Stark AR, et al. Kernicterus: epidemiological strategies for its prevention through systems-based approaches. J Perinatol. 2004; 24:650–62. [PubMed: 15254556]
8. Watchko JF. Hyperbilirubinemia in African American neonates: clinical issues and current challenges. Semin Fetal Neonatal Med. 2010; 15:176–82. [PubMed: 19932984]
9. Watchko JF1, Kaplan M, Stark AR, Stevenson DK, Bhutani VK. Should we screen newborns for glucose-6-phosphate dehydrogenase deficiency in the United States? J Perinatol. 2013; 33:499–504. [PubMed: 23429543]
10. Koopmans J, Friedman Ross L. The Influence of Policy on Physicians' Attitudes Toward Newborn Screening Programs Does Familiarity Breed Acceptance? Pediatrics. 2006; 117:1477–85. [PubMed: 16651300]
11. WHO Working Group. Glucose-6-phosphate dehydrogenase deficiency. Bull World Health Organ. 1989; 67:601–11. [PubMed: 2633878]
12. National Newborn Screening Status Report. http://genes-r-us.uthscsa.edu/sites/genes-r-us/files/nbsdisorders.pdf. Updated January 6, 2013. Accessed January 9, 2014
13. Nock ML, Johnson EM, Krugman RR, Di Fiore JD, Fitzgerald S, Sandhaus LM, Walsh MC. Implementation and analysis of a pilot in-hospital newborn screening program for glucose-6-phosphate dehydrogenase deficiency in the United States. J Perinatol. 2011; 31:112–7. [PubMed: 20539275]
14. Missiou-Tsagaraki S. Screening for glucose-6-phosphate dehydrogenase Deficiency as a preventive measure: prevalence among 1,286,000 Greek newborn infants. J Pediatr. 1991; 119:293–9. [PubMed: 1824550]
15. Padilla CD. Newborn screening in the Philippines. Southeast Asian J Trop Med Public Health. 2003; 34:87–8. [PubMed: 15906705]
16. Padilla CD, Therrell BL. Newborn screening in the Asia Pacific region. J Inherit Metab Dis. 2007; 30:490–506. [PubMed: 17643195]
17. Riskin A, Gery N, Kugelman A, Hemo M, Spevak I, Bader D. Glucose-6-phosphate dehydrogenase deficiency and borderline deficiency: association with neonatal hyperbilirubinemia. J Pediatr. 2012; 161:191–6. [PubMed: 22459229]
18. Pao M, Kulkarni A, Gupta V, Kaul S, Balan S. Neonatal screening for glucose-6-phosphate. dehydrogenase deficiency. Indian J Pediatr. 2005; 72:835–7. [PubMed: 16272653]
19. Joseph R, Ho LY, Gomez JM, Rajdurai VS, Sivasankaran S, Yip YY. Mass newborn screening for glucoe-6-phosphate dehydrogenase deficiency in Singapore. Southeast Asian J Trop Med Public Health. 1999; 30:70–1. [PubMed: 11400790]

20. Mallouh AA, Imseeh G, Abu-Osba YK, Hamdan JA. Screening for glucose-6-phosphate dehydrogenase deficiency can prevent severe neonatal jaundice. Ann Trop Paediatr. 1992; 12:391–5. [PubMed: 1283668]
21. Meloni T, Forteleonl G, Meloni GF. Marked decline of favism after neonatal glucose-6-phosphate dehydrogenase screening and health education: the northern Sardinian experience. Acta Haematol. 1992; 87:29–31. [PubMed: 1585769]
22. Slusher TM, Zipursky A, Bhutani VK. A global need for affordable neonatal jaundice technologies. Semin Perinatol. 2011; 35:185–91. [PubMed: 21641493]
23. Kaplan M, Hammerman C. The need for neonatal glucose-6-phosphate dehydrogenase screening: a global perspective. J Perinatol. 2009; 29:S46–52. [PubMed: 19177059]
24. Beutler E. G6PD: population genetics and clinical manifestations. Blood Rev. 1996; 10:45–52. [PubMed: 8861278]

Table 1

Change in Management of Inpatient and Outpatient Providers

	n = 36 n (%)
More focus on in-hospital counseling about jaundice and the importance of newborn follow-up for hyperbilirubinemia	29 (81%)
Counseling on avoidance of triggers of hemolytic crisis	27 (75%)
Better understanding of risk factors for hyperbilirubinemia for each patient and when to re-admit for treatment	25 (69%)
More bilirubin testing in-hospital	17 (47%)
Earlier newborn follow-up appointments	13 (36%)
More frequent use of home nursing visits	12 (33%)
Extend birth hospitalization length of stay for G6PD deficient babies	4 (11%)
More frequent newborn follow-up appointments	4 (11%)
More bilirubin testing as outpatient	4 (11%)
Other	1 (3%)
More use of home phototherapy	0

Table 2

Change in Management of Outpatient Only Providers

	n = 24 n (%)
Counseling on avoidance of triggers of hemolytic crisis	17 (71%)
Better understanding of risk factors for hyperbilirubinemia for each patient and when to re-admit for treatment	14 (58%)
More bilirubin testing as outpatient	6 (25%)
More frequent newborn follow-up appointments	3 (13%)
Other	2 (8%)
More use of home phototherapy	1 (4%)

Table 3

Open-ended comments

Quality Improvement suggestions:
It looks like the teaching to parents is not heard/understood by most. Most of the parents I see have low health literacy levels.
Sometimes families understand and sometimes they are clueless- not sure what makes the difference but I suspect it is the handout?
Still not clear to the outpatient providers what education is given to families and what to do with the diagnosis when it is received.
Support of program:
This piece of information if very helpful, and I use it almost daily. With our patient population I can't imagine not having this screening
Having the diagnosis helps me in making sure to avoid triggers
Love it!
I think there should be universal screening