Original Paper

Public Health Genomics

Public Health Genomics 2011;14:173–177
DOI: 10.1159/000322527

Received: February 2, 2010
Accepted after revision: November 1, 2010
Published online: December 18, 2010

False Positive Newborn Screening Results Are Not Always Benign

D.R. Morrison[a] E.W. Clayton[b–d]

[a]Department of Sociology, [b]Center for Biomedical Ethics and Society, [c]Department of Pediatrics, and [d]School of Law, Vanderbilt University, Nashville, Tenn., USA

Key Words
Communication · Ethics · False positive · Newborn screening · Stress

Abstract
Objective: Our goal was to assess the impact on families of receiving abnormal newborn screening results. ***Patients and Methods:*** We conducted telephone interviews with parents of 3 groups of children who had received abnormal newborn screening results: (1) false positive but otherwise healthy (FP, n = 28), (2) true positive (TP, n = 20), and (3) false positive with other medical conditions (FP + other, n = 12). Interviews, based on the instruments developed by Waisbren et al. [J Pediatr Psychol 2004;29:565–570], included open- and close-ended questions as well as the Parental Stress Index (PSI). ***Results:*** In response to open ended questions, FP parents expressed concern about having more children and identified numerous problems with how they were told about newborn screening. Parents of FP + other reported the most stress, followed by parents of children with metabolic disease. Nonetheless, almost 10% of FP parents reported clinically significant stress as well as worry about their child's health and future. ***Conclusions:*** False positive newborn screening results cause some parents to experience stress and long-term worry. Although more work is needed to learn how well these sequelae can be averted by more effective communication in the pre- and postnatal periods, these effects need to be considered in deciding whether to add new disorders to newborn screening panels.

Introduction

Newborn screening programs for metabolic and endocrine disorders have recently expanded. Tennessee, like many states, routinely screens for over 40 conditions. This expansion of screening has lead to an increase in the number of affected children identified, but due to variations in validity and reliability of such tests as well as the low frequency of these disorders, the incidence of false positive (FP) rates is even higher [1]. A false positive result is one that initially suggests the presence of disease in a child that is not borne out on further clinical evaluation. False positive results may be resolved by 1 or more repeat screens, which are often performed by the primary care provider, or by more extensive testing. This follow-up is usually requested after the child has left the nursery. A number of studies have demonstrated that some parents whose children need additional screening experience distress and are not reassured by normal results obtained on follow-up [2–6], even though some investigators suggest that parents are willing to tolerate these adverse effects [7]. The research reported here describes how parents whose children received abnormal results experience newborn screening as well as the levels of stress they experienced. We also assessed the impact of the child's overall health status on the level of stress.

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

1662–4246/11/0143–0173$38.00/0

Accessible online at:
www.karger.com/phg

Ellen Wright Clayton, MD, JD
Center for Biomedical Ethics and Society
2525 West End Ave., Suite 400
Nashville, TN 37203 (USA)
Tel. +1 615 322 1186, Fax +1 615 936 3800, E-Mail ellen.clayton@vanderbilt.edu

Table 1. Demographic characteristics of respondents

Group	FP (n = 28)	TP (n = 20)	FP + other (n = 12)
Respondent			
Mother	26 (93%)	18 (90%)	12 (100%)
Newborn gender			
Male	17 (61%)	10 (50%)	9 (75%)
Self-identified race			
White	17 (61%)	17 (85%)	9 (75%)
Black	7 (25%)	1 (5%)	1 (8%)
Other	4 (14%)	2 (10%)	2 (17%)
Hollinghead Index Score (with standard deviation)	17.11 ± 2.1	16.1 ± 1.9	18.08 ± 1.0

FP = False positive newborn screening results; TP = true positive newborn screening results; FP + other = false positive newborn screening results in children with other medical problems.

Patients and Methods

Enrollment and Study Procedures

Genetics and pediatric endocrinology clinics at Vanderbilt University Medical Center (VUMC) receive faxes of all abnormal newborn screening results for infants born in middle Tennessee. These clinics are called about results that exceed the state's 'alarm levels,' which indicate a greater likelihood of disease, so that they can provide support for primary care providers who bring the children in for further testing and remain the parents' primary source of information, particularly if abnormal results turn out to be false positive. Staff at these subspecialty clinics identified 239 sets of parents whose children were born in middle Tennessee and who had either true or 'alarm level' false positive metabolic or endocrine disorder screening results to participate in this study. Clinic staff then sent each household a letter describing the study and 2 copies of informed consent documents. Participants were asked to keep 1 copy and return the other signed consent form and another form that specified a telephone number and best times to call in order to schedule a telephone interview. Parents who did not respond to the initial letter were subsequently invited to participate by phone. The interviewer explained the study in a way that was consistent with the informed consent document. Parents who agreed to be interviewed at that time were mailed a copy of the informed consent document for their records. Parents were offered USD 25 for completing the survey. Respondents were interviewed once. Parents who did not speak English as a first or second language were excluded from the study as were parents whose children had died. Participation rates for this study were approximately 25% overall. Of the families invited to take part in this study, 28 of 79 (35%) families of children with false positive results, 20 of 50 (40%) families of children with true positive results, and 12 of 111 (11%) children with false positive results plus another condition agreed to participate. Respondents varied in the interval between their receipt of newborn screening results and the time of the interview. Although either parent was eligible to participate, almost all respondents were mothers (54/60, 95%). The demographic characteristics of respondents are shown in table 1. The study was approved by the Institutional Review Board of VUMC.

Data Collection

The goal of this study was to assess parents' understanding of and response to their child's newborn screening results using a mixed methods approach. The questionnaire created by Waisbren et al. [8] was used to enhance comparability between studies. Parents completed a structured, closed-ended interview, with questions regarding parental health and child health, understanding of the newborn screening process and demographic information. Most items were answered using a 5-point Likert scale. Parents whose children had FP screens received a shortened version of the interview, including questions about the need for a repeat screen. Parents of children with true positive results were asked a more extensive set of questions that included information about the severity of the child's condition, treatments and therapies received. Social class of each respondent was derived using the 2-category Hollingshead scale, based on level of education and occupational status.

Parents were asked open-ended questions about their experience with newborn screening, their thoughts about having more children and ideas for improving the newborn screening process. Responses to these questions were reviewed and independently coded by both authors using a contextual content analysis framework [9, 10], focusing on identifying key words or phrases that respondents used consistently to describe their experiences with newborn screening. The raters initially agreed on codes 80% of the time; remaining differences between raters were reconciled through a focused review.

Finally, parents were asked to complete the short form of the Parental Stress Index Short Form (PSI-SF). The PSI-SF is a 36-item questionnaire aimed at determining stress in parent-child interactions and designed to be completed by parents. The parental distress subscale determines the distress a parent is experiencing in his or her role as a function of personal factors related to parenting. Items on this subscale include measures of a sense of impaired parenting competence, stress associated with restrictions placed on

other life roles, conflict with the child's other parent, lack of social supports, and the presence of depression [11]. Scores on the parent-child dysfunctional interaction subscale indicate the parent's perceptions that his or her child does not meet the parent's expectations and that the interactions are not reinforcing his or her role as parent. This scale captures parents' feelings that his or her child is a negative element in the parent's life. High scores on this scale suggest that the parent-child bond is either threatened or has not yet been adequately established. The Difficult Child Subscale focuses on the basic behavioral characteristics of children that make them either easy or difficult to manage [11]. Normal ranges for total stress scores is 55–85, with scores >85 suggesting a need for treatment [11, 12]. The alpha reliability coefficients are 0.91 for the total stress score and between 0.8 and 0.87 for the subscale scores. The PSI-SF has a correlation of 0.95 with the longer, full-length PSI [11]. In the 9 cases of missing data in responses to the PSI-SF, mean substitution within the missing item subscale score was used.

Data Analysis

For purposes of analysis, parents were divided into 3 groups: (1) those whose children received FP results but were otherwise healthy (FP), (2) those whose children were diagnosed with a metabolic or endocrine disorder (TP), and (3) those whose children had FP results in addition to other medical problems, ranging from mild to moderate prematurity to congenital heart disease, spina bifida, and gastroschisis (FP + other). The children in the last group varied dramatically in the difficulties they faced both in their newborn course and subsequently. Because the number of cases in each of the 3 comparison groups is not equal, statistical methods that do not require balanced sample sizes were used. Although sample sizes reported here are low, χ^2 analysis in small samples tends to increase the probability of a type II error, failing to reject the null hypothesis when it is in fact false.

Results

Parental Responses to Newborn Screening

Parents made many comments in response to open-ended questions concerning their understanding of newborn screening and its impact. A summary of coding categories across all 3 groups concerning future pregnancies is presented in table 2. While many respondents in the TP and FP groups expressed their fear of recurrence and desire to limit their family size, parents of FP children were more likely than parents of TP children to express a desire for no more children, whereas parents of TP children were more likely to emphasize their fear of recurrence in a future pregnancy. While a few questions were asked of all respondents, we focus primarily on the comments of parents whose children had received FP screening results but were otherwise healthy. Some parents with FP results on newborn screening cited age as an important factor in why newborn screening results changed, whereas others focused on laboratory errors. One parent opined, 'Mixup in the lab or something …,' whereas another focused on the location of the blood draw: 'Maybe because they drew blood instead of pricking her finger.' Another parent cited medical staff error: 'I just think that the people down there [at the hospital] didn't do the test right. They touched his heel to the paper and I understand that they're not supposed to do that …' These comments lead us to believe that parents are not fully informed about the causes of FP results. Had they been more informed, it is likely that many more would have recalled that FP results are an artifact of variation in the specificity and/or sensitivity of screening tests.

Table 2. Content analysis coding: 'How has this affected your thoughts on having more children?'

Code	TP	FP	FP+
Fear of recurrence	8 (47%)	2 (20%)	0
No more children	4 (24%)	4 (40%)	4 (67%)
Uncertain	3 (18%)	2 (20%)	0
Stress or anxiety	2 (12%)	1 (10%)	2 (33%)
Complication	0	1 (10%)	0

TP = True positive newborn screening results; FP = false positive newborn screening results; FP+ = false positive newborn screening results in children with other medical problems.

Parents of children with FP results on newborn screening also expressed both ambivalence and fear when asked their thoughts about future pregnancies. One parent, expressing her desire and reservations, said, 'I want more children but I am scared … It's [the FP newborn screen] has affected the idea [of having more children].' Another expressed her uncertainty and financial worries should a future child carry a genetic or other disorder: 'Well, you don't know what to expect, and I'm staying in my job because of the insurance.' This mother summed up the thoughts of several parents when she said, '[I] don't plan to have any more. [I] don't want to take a chance of it happening again …'

Parents with FP results also reported that they wanted more information about the newborn screening process and what the 'next steps' were if a diagnosis was suspected but not yet confirmed. One parent said, '… I think it would have been more helpful to know about newborn screening before I gave birth because I get really emotional after delivery …' A second mother also suggests that more education is needed: 'Maybe somebody could have explained a bit more about why it came back [suggesting a biochemical genetic disorder], what could have been the causes for

Table 3. Summary data for Parental Stress Index-Short Form (PSI-SF)

	Mean	SD	Range
Total sample	73.9	22.0	43–130
FP (n = 28)	68.4	16.3	43–115
TP (n = 20)	74.5	22.0	47–115
FP + other (n = 12)	85.9	29.7	44–130

FP = False positive newborn screening results; TP = true positive newborn screening results; FP + other = false positive newborn screening results in children with other medical problems.

it … and what we could do if the next one came back [positive for a biochemical genetic disorder] also.' Another pointed to what she felt was provider error: 'Him passing it, and him not having to re-test and re-test. I did get some specific information as to what the concern was … Just the pure discomfort of having his heel stuck each time.' Many parents identified the need for more education and resources in understanding what the newborn screening tests for, and about the possibility of false positive results.

Table 3 summarizes the impact of screening results on parental stress. Mean scores on the PSI-SF were 73.9 for the entire sample, 68.4 for the FP group, 74.5 for the TP group, and 85.9 for the FP + other factor group.

T-test analysis for mean differences in total PSI-SF scores revealed a statistically significant difference at the $p < 0.05$ level between FP and FP+ groups, but no statistically significant differences in other pair-wise comparisons. Examination of the subparts of the PSI-SF stress score through analysis of variance also revealed statistically significant differences between FP and FP + other on the Difficult Child Subscale score at the $p < 0.05$ level, and results that tend towards significance on the total parental stress score. While results on the Difficult Child Subscale score, by themselves, do not indicate a clinically significant level of parental stress, this additional analysis of the parental stress data helps researchers understand which aspect of parenting is most challenging. Similarly, in response to a series of Likert-scale probes, parents of children who were FP + other were more likely to report that their children required extra care and that they were concerned about their child's health and future (all $p < 0.05$). Even so, approximately 10% of FP parents reported that their child required extra care and they were worried about their child's health can future.

In our sample, approximately 7% of respondents (n = 2) in the FP group reported clinically significant levels of parental stress. This was lower than both the TP group, with 30% reporting clinical levels of stress (n = 6), and the FP + other group, where 58% reported clinically significant levels of stress (n = 7). Although the absolute numbers of respondents exhibiting clinically significant levels of stress are low, at least some in each group were affected. Since the likelihood of such extreme stress is unlikely to be equally distributed among study groups, these findings were then compared using χ^2 with prior reports by other investigators regarding stress and FP, TP and children who are otherwise affected, respectively. Gurian et al. [12] reported that 11% of mothers with FP children reported clinically significant levels of stress. In Waisbren et al.'s [8] study of parenting stress associated with having children with biochemical genetic disorders, 32% of parents whose children had metabolic disorders reported clinically significant levels of stress. Singer et al. [13], who used the full-length PSI, reported that 32% of very low-birth weight reported clinically significant symptoms of overall distress in contrast with 17% of mothers of term infants. In each case, comparisons with our findings revealed no significant differences.

Discussion

Our findings reaffirm that FP newborn screening results are not entirely benign even when children are otherwise healthy [14], consistent with the findings by investigators in the Northeast and upper Midwest of the United States [5, 8]. This study contributes to the existing literature by reporting parents' explanations of why their infants' false positive results resolved. While many parents simply did not know why their child's results changed, others attributed the change to their child's growth and maturation. Others felt that maternal health contributed to the original FP result. A smaller set of parents blamed a new test, laboratory errors and test procedures. One explicitly mentioned the power of religious faith. None of these rationales is consistent with current scientific knowledge. Only 2 out of 28 FP parents reported that the normal follow-up result did not represent a change in the child's development or a prior laboratory error. These findings point to significant opportunities for doctors and genetics professionals to educate parents before and after the newborn screening process [3, 15, 16].

FP parents also were uncertain about the degree to which newborn screening processes could be made more positive and helpful. Several parents reported a desire for more timely information about newborn screening tests.

Parents expressed the need to be made aware of newborn screening tests prior to delivery, a recommendation that has been made by many others [17, 18]. Common concerns for this group of parents included anxiety associated with waiting for test results [4] as well as worry about the proper way to feed and care for their newborn in light of an uncertain diagnosis. Additionally, parents expressed a need for reassurance and discussion about the meaning of newborn test results.

With respect to future pregnancies, many parents with FP results were concerned about the likelihood of future false positives and the stress of waiting for lab results that may be inconclusive, in some cases saying that the experience led them to avoid future childbearing [5]. That parents of TP children were no more likely to express a desire *not* to have any more children, despite their citing the stress, expense and anxiety associated with the possibility of recurrence in future pregnancies, is consistent with earlier reports that parents differ widely in the impact of having a child with a metabolic disorder on future procreation [19–22].

While the relatively small number of respondents who were interviewed at varying lengths of time after their infants had received newborn screening results is a drawback of this study, the levels of confusion and concern that emerged were striking. The lack of normal controls does not detract from our findings, which are focused on the impact of abnormal newborn screening results.

Clearly, more attention needs to be paid to communication with parents, both before newborn screening occurs and while abnormal results are being evaluated [3]. Even with the best of efforts, however, it seems unlikely that all parents whose children receive false positive screening results can be completely reassured. As proposals to screen newborns for additional disorders are considered, it will be critical to weigh the real risks of adverse sequelae from false positive screening results in the balance.

Acknowledgments

This research was funded by March of Dimes Impact of Newborn Screening on Families, March of Dimes, 6-FY05-85. We would like to thank Susan Waisbren for sharing her questionnaire with us, Emily Tanner-Smith for research assistance, Susan Wilkins and Marilee Weingartner for identifying potential participants, and Kyle Brothers for his helpful comments.

References

1 Tarini BA, Christakis DA, Welch HG: State newborn screening in the tandem mass spectrometry era: more tests, more false-positive results. Pediatrics 2006;118:448–456.
2 Fyro K, Bodegard G: Four-year follow-up of psychological reactions to false positive screening tests for congenital hypothyroidism. Acta Paediatr Scand 1987;76:107–114.
3 Howell RR: The high price of false positives. Mol Genet Metab 2006;87:180–183.
4 Tluczek A, Koscik RL, Farrell PM, Rock MJ: Psychosocial risk associated with newborn screening for cystic fibrosis: parents' experience while awaiting the sweat-test appointment. Pediatrics 2005;115:1692–1703.
5 Tluczek A, Mischler EH, Bowers B, Peterson NM, Morris ME, Farrell PM, Bruns WT, Colby H, McCarthy C, Fost N, et al.: Psychological impact of false-positive results when screening for cystic fibrosis. Pediatr Pulmonol Suppl 1991;7:29–37.
6 Waisbren SE, Albers S, Amato S, Ampola M, Brewster TG, Demmer L, Eaton RB, Greenstein R, Korson M, Larson C, Marsden D, Msall M, Naylor EW, Pueschel S, Seashore M, Shih VE, Levy HL: Effect of expanded newborn screening for biochemical genetic disorders on child outcomes and parental stress. JAMA 2003;290:2564–2572.
7 Prosser LA, Ladapo JA, Rusinak D, Waisbren SE: Parental tolerance of false-positive newborn screening results. Arch Pediatr Adolesc Med 2008;162:870–876.
8 Waisbren SE, Rones M, Read CY, Marsden D, Levy HL: Brief report: predictors of parenting stress among parents of children with biochemical genetic disorders. J Pediatr Psychol 2004;29:565–570.
9 McTavish DG, Pirro EB: Contextual content analysis. Qual Quant 1999;24:245–265.
10 Krippendorf K: Content Analysis: An Introduction to Its Methodology. Thousand Oaks, Sage Publication, 2004.
11 Abidin RR: Parenting Stress Index (PSI), ed 3. Odessa, Psychological Assessment Resources, 1995.
12 Gurian EA, Kinnamon DD, Henry JJ, Waisbren SE: Expanded newborn screening for biochemical disorders: the effect of a false-positive result. Pediatrics 2006;117:1915–1921.
13 Singer LT, Salvator A, Guo S, Collin M, Lilien L, Baley J: Maternal psychological distress and parenting stress after the birth of a very low-birth-weight infant. JAMA 1999;281:799–805.
14 Hewlett J, Waisbren SE: A review of the psychosocial effects of false-positive results on parents and current communication practices in newborn screening. J Inherit Metab Dis 2006;29:677–682.
15 Clayton EW: Talking with parents before newborn screening. J Pediatr 2005;147(suppl 3):S26–29.
16 Kemper AR, Fant KE, Clark SJ: Informing parents about newborn screening. Public Health Nurs 2005;22:332–338.
17 Genetics Committee: ACOG committee opinion number 287, October, 2003: newborn screening. Obstet Gynecol 2003;102:887–889.
18 Newborn Screening Task Force: Serving the family from birth to the medical home. A report from the newborn screening task force convened in Washington DC, May 10–11, 1999. Pediatrics 2000;106:383–427.
19 Dudding T, Wilcken B, Burgess B, Hambly J, Turner G: Reproductive decisions after neonatal screening identifies cystic fibrosis. Arch Dis Child Fetal Neonatal Ed 2000;82:F124–F127.
20 Helton JL, Harmon RJ, Robinson N, Accurso FJ: Parental attitudes toward newborn screening for cystic fibrosis. Pediatr Pulmonol Suppl 1991;7:23–28.
21 Mischler EH, Wilfond BS, Fost N, Laxova A, Reiser C, Sauer CM, Makholm LM, Shen G, Feenan L, McCarthy C, Farrell PM: Cystic fibrosis newborn screening: impact on reproductive behavior and implications for genetic counseling. Pediatrics 1998;102:44–52.
22 Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS: Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. Health Technol Assess 2004;8:iii, ix–x, 1–109.