The Effects of False-positive Result in Newborn Congenital Hypothyroidism Screening to Parents in Guangxi, China

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Abstract

Background: As more than 200,000 neonates participate in newborn congenital hypothyroidism (CH) screening in Guangxi each year, the overall number of false positives has increased. Concerns arise regarding the potential demographic impact on parental stress and knowledge of CH results has emerged.

Methods: 255 parents were invited to participate in the false-positive (FP) group, and 1040 parents were invited to participate in the control group. After providing consent, the parents completed a semistructured questionnaire on demographic characteristics, knowledge of CH and the parental stress index-short form (PSI-SF).

Results: The parents in the FP group had better knowledge of CH and higher PSI scores than did the parents in the control group (both $P<0.001$). The result of Logistic Regression showed that the major influence factors of knowledge of CH were FP experience and source of knowledge (both $P<0.001$). The parents in the FP group who were well-informed during the recall phone call had lower PSI scores than did the other parents ($P = 0.001$). The results suggested that FP screening results may affect parental stress and the parent-child relationships.

Conclusion: Targeted health education should be carried out to increase prospective parents' knowledge of NBS and reduce parental stress when false-positive results are received.

Background

Newborn screening (NBS) is a public health program that enables the presymptomatic identification and early treatment of certain diseases and disorders in the first weeks of life [1]. To identify congenital defects, NBS was first debuted in America in 1961, and it was first introduced in China in the early 1980s [2]. Although the testing programs and testing protocols differed among provinces, the congenital hypothyroidism (CH) and phenylketonuria (PKU) were the most commonly screened programs in China [3]. CH is a condition of thyroid hormone deficiency that becomes apparent after birth, and severe CH can lead to growth failure and permanent intellectual disability, which may lead to a heavy burden on the family [4]. Early diagnosis and timely intervention will yield better prognosis and reduce healthcare costs for CH patients. In line with the common practice worldwide, the neonates with positive NBS results in China were recalled for follow-up test and asked for a pediatricians consultant as soon as possible [5]. Parents who receive a positive NBS result experience a long-lasting psychological change, even several months after they find out the result was a false-positive (FP) [6]. However, little is known about the psychological effect of parents who received FP NBS results for CH in Guangxi *Zhuang* Autonomous region, China.

The Guangxi *Zhuang* Autonomous region is located in southern China, with more than 56.95 million people of various ethnicities and cultures. The Guangxi Newborn Screening Center (GX-NBSC) was established in 2009, and is responsible for screening more than 200,000 blood samples each year. The

NBS programs in Guangxi include CH, PKU, congenital adrenal hyperplasia (CAH), glucose-6-phosphate dehydrogenase (G6PD) deficiency, thalassemia, congenital deafness and inherited metabolic diseases (IMD) by tandem mass. The thalassemia and G6PD deficiency are strongly recommended programs in Guangxi due to the high prevalence, however, most of the neonates with abnormal NBS results were mild and not life-threatening [7, 8]. Previous studies have reported that the prevalence of CH in Guangxi is 1/1694, and the incidence is slightly higher than the average level around the world [9]. Each year, thousands of neonates are found to have an elevated thyroid stimulating hormone (TSH) level in the initial NBS test in Guangxi; moreover, less than 5% of them are diagnosed with CH, which implies that most of the results are FPs [10]. Therefore, we study the psychological effects of FP results in NBS for CH and its relevant knowledge in parents of Guangxi by conducting a questionnaire, in order to provide targeted health education and reduce psychological stress.

Methods

Study design and site

In China, the standard flow of NBS is as follow (Fig. 1): (a) collect the heel blood 72 h after breastfeeding (no more than a week); (b) perform the NBS and provide the results within 10 days; (c) make a phone call to recall the neonate immediately if abnormality (e.g. positive result, contaminated blood spot) occurs; (d) the first physical exam for neonates is recommended at 42 days after birth. The parents whose neonates had abnormal NBS result were asked for a retest in GX-NBSC as soon as possible, and the retest result would be provided within 24 h. The parents would not receive phone call from GX-NBSC if the NBS results were within normal reference ranges, and most of them preferred to fetch the report during the first physical exam for neonates. Therefore, we conducted our investigation at this time.

Mothers and fathers of neonates were invited to participate in our investigation by referral of the pediatricians, then the parents who met the inclusion criteria but not met the exclusion criteria were interviewed by our well-trained nurses. For a family, either mother or father was invited. The inclusion criteria for FP group were the parents of neonates whose initial result was abnormal or inconclusive for CH screening and negative in follow-up diagnosis; for control group were the parents of neonates whose initial results were all within the normal reference ranges. The exclusion criteria were as follows: (a) mothers of neonates with thyroid malfunction or mothers who took drugs that can affect thyroid function during pregnancy, (b) parents of neonates who were born at less than 32 weeks of gestation or diagnosed with severe health problems and (c) parents of neonates were unable to communicate. During September 1 to October 30, 2020, 411 parents met the inclusion criteria for FP group and 1684 parents met inclusion criteria for control group, 135 and 612 parents refused our invitation respectively, 19 and 28 parents met the exclusion criteria respectively. After ruled out the spoiled questionnaires, 255 and 1040 valid questionnaires of FP group and control group respectively were analyzed in this study (Fig. 2). All the participants were signed the informed consent forms. This study was approved by the Institutional Review Board of Guangxi University of Chinese Medicine (No. GXUCM_IRB_H_2019-11-01-1). Participants

or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Data collection

The interview was completed and tape recorded by our well-trained nurses. The semistructured questionnaires were scored by three researchers who were blinded to the group identities. The questionnaire consisted of 3 section on the following topics: "demographic characteristics", "knowledge of NBS", and "psychological situations". The first section was designed to collect demographic data, including sex, age, ethnicity, educational year, annual household income and living area *etc*. In the second section, there are 10 questions included the knowledge on cause, symptoms, treatment and diagnosis of CH, and 1 multiple-choice question for the source of knowledge. The questions in the last part regarded the parents' feelings after the recall phone call and questions for the parenting stress index-short form (PSI-SF) (Chinese version) to assess their feelings.

In the second part, 1 point for a correct answer, zero for the wrong answer. The parent who got 6 points or more was considered to have relevant knowledge of CH; otherwise, they were considered to not have relevant knowledge (score range: 0 to 10). After the interview, the pediatricians would provide a health education on CH, especially for the incorrect questions. For the parents who have multiple sources of knowledge, we repeated them multiple times into different groups.

The PSI-SF (Chinese version) was described previously [11], which includes 36 items and provides a total stress score with 3 subscale scores on the following domains: parental distress, parent-child dysfunctional interactions, and difficult child behavior. Each item was rated on a 5-point Likert scale, with response options ranging from totally agree to totally disagree. The normal range for the total stress score is 55 to 85; scores greater than 85 indicate that the parent needs clinical treatment, while scores less than 10 indicate that the result is questionable. If the parent who scored greater than 85 points, a psychiatrist referral to provide psychological help.

Data analyses

The quantitative data are presented as means ± SEMs; the descriptive data are presented as frequencies and percentages. IBM SPSS Statistics software (version 26.0, Chicago, USA) was used for data analysis. The age of the parents was analyzed by Student's unpaired *t*-test, and other demographic characteristics were analyzed by using the Wilcoxon rank-sum test for continuous and scale variables and Fisher's exact test for dichotomous variables. Student's unpaired *t*-test was also used to compare the knowledge of NBS and PSI scores between groups. For the PSI scores, subjects who failed the defensive response index (< 10) were excluded from the analyses. All *P* values were 2-sided, and values of < 0.05 were considered significant.

Results

Sample characteristics

The characteristics of the participants are reported in Table 1. In the FP group, 121 mothers and 137 fathers of 124 daughters and 134 sons were included. The average age of the parents was 28.87 ± 5.84 years. In the control group, 500 mothers and 540 fathers of 509 daughters and 531 sons were included. The average age of the parents was 28.98 ± 5.32 years-old. The sex, age, ethnicity, number of children, education year, living area and annual household income did not significantly differ between these two groups. Thus, the family demographic variables did not need to be controlled for in subsequent analyses.

Table 1
The demographic characteristics of participants [N (%)]

Variable	**FP group (n = 258)**	**Control group (n = 1040)**	χ^2/t	*P*
Age of parents (year)	28.87 ± 5.84	28.98 ± 5.32	0.29	0.770
Sex of parents (female)	121(46.9)	500(48.1)	0.11	0.735
Sex of neonates (female)	124(48.1)	509(48.9)	0.06	0.800
First child (yes)	201(77.9)	792(76.2)	0.353	0.552
Ethnicity				
Han	128(49.6)	524(50.4)	1.73	0.479
Zhuang	123(47.7)	472(45.4)		
Other	7(2.7)	44(4.2)		
Education year				
≤ 9	83(32.2)	391(37.6)	5.04	0.080
10–14	100(38.7)	329(31.6)		
> 14	75(29.1)	320(30.8)		
Living area				
Rural	145(56.2)	517(49.7)	3.48	0.062
City	113(43.8)	523(50.3)		
Annual household income (yuan)				
< 50,000	74(28.7)	316(30.4)	0.47	0.792
50,000-100,000	145(56.2)	560(53.8)		
> 100,000	39(15.1)	164(15.8)		

Relevant knowledge of CH

The parents in the FP group had a higher correctness rate for every question than did those in the control group, especially in clinical symptoms and treatment and prevention part (all $P < 0.001$). The parents in the FP group had higher scores than did the parents in the control group ($t = 20.26$, $P < 0.001$), which indicated that they had more relevant knowledge of CH. According to our criteria (the one who got 6 or more points), 324 parents were considered to have relevant knowledge of CH, that was 140 in the FP group (54.26%) and 184 in the control group (17.69%) respectively (Table 2).

Table 2
The parents' awareness of relevant knowledge of congenital hypothyroidism (CH) [N (%)]

Questions (correct answer)	**FP group (n = 258)**	**Control group (n = 1040)**	χ^2/t	*P*
Causes				
The incidence of CH may associated with the father's smoking and drinking behaviors (No)	106(41.1)	364(35.0)	3.31	0.069
The incidence of CH may associated with the maternal iodine intake (Yes)	145(56.2)	519(49.9)	3.28	0.070
The incidence of CH is totally determined by genes (No)	134(51.9)	457(43.9)	5.33	0.021
Clinical symptoms				
Most newborns have no obvious clinical symptoms of CH at first beginning (Yes)	224(86.8)	156(15.0)	515.0	< 0.001
No clinical symptoms means no harm to CH children (No)	173(67.0)	105(10.1)	398.5	< 0.001
CH is an endocrine disease and does not affect children's intelligence (No)	202(78.3)	87(8.4)	584.1	< 0.001
Treatments and Preventions				
The thyroidectomy can cure CH for good (No)	93(36.0)	211(20.3)	28.62	< 0.001
Some CH children have to use medication all their lives (Yes)	130(50.4)	368(35.4)	19.68	< 0.001
Eat appropriate iodine products during pregnancy can prevent CH to a certain extent (Yes)	177(68.6)	547(52.6)	21.48	< 0.001
Genetic counselling can help to prevent CH (No)	180(69.8)	419(40.3)	72.29	< 0.001
Score	6.06 ± 2.26	3.11 ± 2.05	36.64	< 0.001

Subsequently, the source of knowledge were investigated. Due to some parents had multiple sources of knowledge and we repeated them into different groups, the total amount was greater than the interviewed parents. Most parents reported that they acquire the relevant knowledge from the internet, including Wechat public account, Sina Weibo or Bulletin Board System (n = 574, 44.22%); followed by from hospitals or doctors (n = 318, 24.50%), family members or friends (n = 268, 20.65%), publications (n = 107, 8.24%) and other sources (n = 31, 2.39%). However, the parents who acquire relevant knowledge from hospitals or doctors had highest awareness rate than the other groups (n = 112, 35.22%).

In order to find out the factors that influence the parental awareness rate of relevant knowledge of CH among 1298 parents, we compared the difference between different demographic characteristics, FP experience and source of knowledge (Table 3). The FP experience (χ^2 = 147.6, P < 0.001), source of knowledge (χ^2 = 70.57, P < 0.001), education year (χ^2 = 9.40, P = 0.009) and first child or not (χ^2 = 4.40, P = 0.036) were significant correlated with the awareness rate. Take the “awareness rate” as the independent variable and take the “FP experience”, “source of knowledge”, “education year” and “first child” as the dependent variable into the Logistic Regression. As a result, the FP experience and the source of knowledge were the major influence factors to parental awareness rate of relevant knowledge of CH (both P < 0.001) (Table 4).

Table 3
The influence factors of parents' relevant knowledge of congenital hypothyroidism (CH) [N (%)]

Variable	Knowledge of CH	χ^2	*P*
Age of parents (year)			
< 25	84(23.9%)	5.45	0.066
25–35	167(27.8%)		
> 35	73(21.2%)		
Sex of parents			
Male	168(24.8%)	0.02	0.898
Female	156(25.1%)		
Sex of neonates			
Male	163(24.5%)	0.09	0.766
Female	161(25.4%)		
First child			
Yes	234(23.6%)	4.40	0.036
No	90(29.5%)		
Ethnic			
Han	163(25.0%)	0.19	0.909
Zhuang	147(24.7%)		
Other	14(27.5%)		
Education year			
≤ 9	97(20.5%)	9.40	0.009
10–14	111(25.9%)		
> 14	116(29.4%)		
Living area			
Rural area	151(22.8%)	3.34	0.068
Urban area	173(27.2%)		
Annual household income (yuan/year)			
< 50,000	97(24.9%)	2.04	0.361

Variable	Knowledge of CH	χ^2	*P*
50,000-100,000	184(26.1%)		
> 100,000	43(21.2%)		
False-positive experience			
Yes	140(54.3%)	147.6	< 0.001
No	184(17.7%)		
Source of knowledge			
Hospitals or doctors	112(35.2%)	70.57	< 0.001
Internet	168(29.3%)		
Family member or friends	37(13.8%)		
Publications	6(5.6%)		
Other	1(3.2%)		

Table 4
The Logistic Regression analysis of the influence factors to parental awareness of relevant knowledge of congenital hypothyroidism (CH)

Items	*B*	S.E.	Wald	*df*	Sig.	Exp(*B*)	95% CI for EXP(*B*)	
							Lower	Upper
First child (Yes)	0.428	0.283	2.28	1	0.131	1.534	0.881	2.67
Education year (≤ 9)			4.79	2	0.247			
Education year (10–14)	0.414	0.301	1.89	1	0.169	1.513	0.838	2.729
Education year (> 14)	0.602	0.465	1.68	1	0.195	1.826	0.734	4.541
False-positive experience (Yes)	-5.562	0.524	112.84	1	< 0.001	0.004	0.001	0.011
Source of Knowledge (Hospitals or doctors)			39.99	4	< 0.001			
Source of Knowledge (Internet)	-1.41	0.871	2.62	1	0.105	0.244	0.044	1.345
Source of Knowledge (Family member or friends)	-3.207	0.507	29.97	1	< 0.001	0.04	0.015	0.109
Source of Knowledge (Publications)	-3.475	0.560	31.01	1	< 0.001	0.031	0.01	0.093
Source of Knowledge (Other)	-5.302	0.470	13.21	1	< 0.001	0.005	0.002	0.013
Constant	1.478	0.691	4.57	1	0.033	4.383		

Parental response and parental stress

The parents in the FP group received a recall phone call directly from GX-NBSC when the result of the initial newborn screening test was positive. Our retrospective investigation showed that 122 parents felt anxious (47.29%), and followed by panicked (n = 49, 18.99%), worried (n = 49, 18.99%), concerned (n = 30, 11.63%) and distrustful (n = 13, 5.04%) after receiving the phone call. Even after well-trained pediatricians provided information on the phone call, most parents only remember being asked to bring their neonates to the hospital but did not understand why, even could not recall the name of disease (n = 123, 47.67%). A total of 34.50% of parents totally understood the situation and what to do during the phone call, some of them searched the internet with the key word “congenital hypothyroidism” (n = 89). The rest of the parents did not care what the pediatricians said or blindly believed that their neonates did not have any health

issues (n = 46, 17.83%). All parents took their neonates for follow-up tests, and the tests were performed an average of 3.81 ± 2.59 days after the parents received the phone call.

Because the PSI scores for subjects whose defensive responding index was > 10 were included in the analysis, 1 mother and 2 fathers were excluded from the FP group, and 2 mothers and 3 fathers were excluded from the control group. As shown in Table 5, both the mothers and fathers in the FP group reported higher overall stress on the PSI than did those in the control group (mothers: $t = 15.85$, $P < 0.001$; fathers: $t = 11.43$, $P < 0.001$). In the FP group, 11 mothers (9.17%) and 1 father (0.74%) had scores higher than 85, which indicated that they needed psychological services. However, no parents in the control group had scores within the clinical range. The differences between groups were more pronounced in the total score, parent-child dysfunctional interaction subscales, and difficult child subscales than in the parental distress subscales (all $P < 0.01$). Most mothers and fathers in the same group showed similar scores on PSI scores; however, the mothers in the FP group had higher scores on the parent-child dysfunction interaction subscale than did the fathers ($t = 2.51$, $P = 0.013$). The parents in the FP group who understood the situation well after the recall phone call had lower PSI scores than did the rest of the parents in the FP group (70.7 ± 8.5 *vs.* 73.9 ± 7.3, $t = 3.24$, $P = 0.001$). The PSI scores did not significantly differ among parents with different awareness rate of knowledge and demographic characteristics (all $P > 0.05$).

Table 5
Parenting Stress Index (PSI) Scores for False-Positive (FP) and Control Groups (Mean ± SEM)

Variable	FP group (M/F = 135/120)	Control group (M/F = 537/498)	*t*	*P*
Total score				
Mothers	73.7 ± 7.8	61.9 ± 7.2	15.85	< 0.001
Fathers	71.8 ± 8.2	63.3 ± 7.6	11.43	< 0.001
Parental distress subscale				
Mothers	28.1 ± 5.0	25.1 ± 5.3	5.626	< 0.001
Fathers	27.3 ± 5.5	25.9 ± 4.9	2.893	0.0039
Difficult child subscale				
Mothers	25.8 ± 4.8	20.7 ± 4.0	12.04	< 0.001
Fathers	25.9 ± 5.2	21.3 ± 4.1	11.00	< 0.001
Parent-child dysfunction interaction subscale				
Mothers	19.8 ± 3.7	16.1 ± 3.2	11.02	< 0.001
Fathers	18.6 ± 3.9	16.2 ± 2.4	9.013	< 0.001

There were 3 mothers and 5 fathers were excluded due to their PSI scores were < 10. Abbreviations: F: female; M: male

Discussion

To the best of our knowledge, this is the first psychological survey in parents of neonates who had FP results in the initial newborn CH screening test in China. Compared with the parents in the control group, the parents in the FP group had better knowledge of CH and had higher PSI scores. The awareness rate of knowledge was associated with the FP experience and source of knowledge, while the PSI score was correlated with information acceptability during recall phone call.

The awareness rate of knowledge of CH was 24.96% in all participated parents, and it did not seem like a high number. The possible reason for the low awareness rate may be the low incidence rate of CH, and

parents did not paid as much attention to thalassemia or G6PD deficiency as CH. Therefore, health education on CH or NBS should be carried out in parents of neonates. The parents in the FP group had more relevant knowledge of CH than did the parents in the control group, and the highest contributing factor to this difference was whether they had FP experience. The stress from FP experience motivated parents to acquire more knowledge of CH, which is very common in education [12]. Although more parents acquired the relevant knowledge from internet, the parents who acquired them from hospital or doctors had higher awareness rate. This indicated that the new media is easier to be accepted by the public, but existed with both health misinformation and real-information; meanwhile the knowledge from hospitals is authentic, but the publicity needs to be strengthened [13]. Therefore, hospitals should play a important role in targeted health education by using new media method, in order to increase the knowledge of NBS among all prospective parents. On the other hand, another good timing for health education is during the recall phone call. Previous studies have shown that improved communication and health education can reduce the parental stress and anxiety caused by FP NBS results [14]. Similar to a previous study, we found that the parents in the FP group who were well informed during the recall phone call had lower PSI scores. However, due to the rampant telecom fraud in China, some parents thought the recall phone may be the scam call and did not believe whatever the pediatricians said [15]. Therefore, the pediatricians have to improve their communication skills to make the parents to believe them on the phone.

A FP NBS result indicates dysfunction when dysfunction is not present, which can improve parental knowledge of CH to some extent but lead to other negative outcomes, such as anxiety and stress in parents of neonates, even after the neonate is confirmed to be in good health by follow-up tests [16]. Previous studies have demonstrated that the PSI scores of mothers of neonates who had FP NBS results for cystic fibrosis were higher than those of the control group, and some psychosocial responses could not be detected until 1 year later [17]. In the parents of 173 infants with FP results and the parents of 67 children with normal screening results, Gurian EA *et al.* found that the FP results of expanded NBS may affect parental stress and parent-child relationships [14]. Studies indicate that high-quality parental education and communication may have a positive impact on parents' stress and anxiety, including those who receive FP results [18]. In a previous study in China, the parents of neonates with FP results of expanded NBS had higher PSI scores than did the parents in the normal screening result group, but the demographic differences in the PSI scores have never been studied [6]. Unfortunately, we did not find any effects of the demographic characteristics of parents in Guangxi on the PSI scores. In our study, we found that the PSI scores were higher in the parents of the FP group, which is consistent with the results of previous studies. As we know from the tape, parents in FP group had more questions about their neonates, while the parents in control group had more relaxed conversation in the interview. The difference of voice, speed and tone of speak may reflected the clinical manifestation in parents with different scores of PSI. On the other hand, the FP results affected parent-child relationships to a greater extent among mothers than among fathers, which may due to the previous one-child policy (1982–2015) and present two-child policy (2015-till now) in China.

Our study has some limitations. First, we only retrospectively investigated parental stress on day 42. How long will it take for the parental stress in the FP group to return to normal? Long-term investigations are needed. Second, some health interventions could be added at certain time points. NBS education could be carried out before NBS or during the recall phone calls, and at which time point the educational session is more efficacious could be evaluated. Third, the PSI score of parents whose neonates had true positive result was missing. In practice, since those parents were few and most of them were unwilling to cooperate, they were not included in our study. In addition, some parents met the inclusion criteria but refuced to participate in our investigation, which may induce selection bias.

Conclusions

The results of this study suggest that parents in Guangxi have higher PSI scores when their neonates had FP CH results. The FP experience improved the relevant knowledge of CH among parents, but it had some negative consequences. Targeted health education should be carried out before NBS or during recall phone calls to increase the knowledge of NBS among all prospective parents and reduce parental stress when FP results are received.

Abbreviations

CH: congenital hypothyroidism; FP: false-positive; NBS: newborn screening; PSI-SF: parenting stress index-short form

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Guangxi University of Chinese Medicine (No. GXUCM_IRB_H_2019-11-01-1). All participants provided written informed consent. This investigation was anonymous and confidential, and did not involve personally identifiable information.

The study methods were performed in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and material

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

ST and CL prepared the tables and figures, and wrote the main manuscript text; XZ collected the data; CJ, BW and CL analyzed the data; XW and JM revised the manuscript. All authors reviewed the manuscript.

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References

1. Urv TK, Parisi MA: **Newborn Screening: Beyond the Spot**. *Adv Exp Med Biol* 2017, **1031**:323-346.
2. Fabie NAV, Pappas KB, Feldman GL: **The Current State of Newborn Screening in the United States**. *Pediatr Clin North Am* 2019, **66**(2):369-386.
3. Deng K, He C, Zhu J, Liang J, Li X, Xie X, Yu P, Li N, Li Q, Wang Y: **Incidence of congenital hypothyroidism in China: data from the national newborn screening program, 2013-2015**. *J Pediatr Endocrinol Metab* 2018, **31**(6):601-608.
4. Gruters A, Krude H: **Detection and treatment of congenital hypothyroidism**. *Nat Rev Endocrinol* 2011, **8**(2):104-113.
5. Zhong K, Wang W, He F, Wang Z: **The status of neonatal screening in China, 2013**. *J Med Screen* 2016, **23**(2):59-61.
6. Tu WJ, He J, Chen H, Shi XD, Li Y: **Psychological effects of false-positive results in expanded newborn screening in China**. *PLoS One* 2012, **7**(4):e36235.
7. Nong X, Xu G, Li J, Liang J, Zhong S, Liu C, Wang C: **[Study of the genotypic and hematological feature of hemoglobin H disease in West Guangxi area]**. *Zhonghua Yi Xue Yi Chuan Xue Za Zhi* 2020, **37**(12):1326-1330.
8. Fu C, Luo S, Li Q, Xie B, Yang Q, Geng G, Lin C, Su J, Zhang Y, Wang J *et al*: **Newborn screening of glucose-6-phosphate dehydrogenase deficiency in Guangxi, China: determination of optimal cutoff value to identify heterozygous female neonates**. *Sci Rep* 2018, **8**(1):833.
9. Fu C, Luo S, Li Y, Li Q, Hu X, Li M, Zhang Y, Su J, Hu X, Chen Y *et al*: **The incidence of congenital hypothyroidism (CH) in Guangxi, China and the predictors of permanent and transient CH**. *Endocr Connect* 2017, **6**(8):926-934.
10. Fu C, Luo S, Long X, Li Y, She S, Hu X, Mo M, Wang Z, Chen Y, He C *et al*: **Mutation screening of the GLIS3 gene in a cohort of 592 Chinese patients with congenital hypothyroidism**. *Clin Chim*

Acta 2018, **476**:38-43.

11. Yeh CH, Chen ML, Li W, Chuang HL: **The Chinese version of the Parenting Stress Index: a psychometric study**. *Acta Paediatr* 2001, **90**(12):1470-1477.
12. Wang W, Xu H, Wang B, Zhu E: **The Mediating Effects of Learning Motivation on the Association between Perceived Stress and Positive-Deactivating Academic Emotions in Nursing Students Undergoing Skills Training**. *J Korean Acad Nurs* 2019, **49**(4):495-504.
13. Safarnejad L, Xu Q, Ge Y, Krishnan S, Bagarvathi A, Chen S: **Contrasting Misinformation and Real-Information Dissemination Network Structures on Social Media During a Health Emergency**. *Am J Public Health* 2020, **110**(S3):S340-s347.
14. Gurian EA, Kinnamon DD, Henry JJ, Waisbren SE: **Expanded newborn screening for biochemical disorders: the effect of a false-positive result**. *Pediatrics* 2006, **117**(6):1915-1921.
15. Zheng YJ, Zhou XH, Sheng WG, Xue Y, Chen SY: **Generative adversarial network based telecom fraud detection at the receiving bank**. *Neural Netw* 2018, **102**:78-86.
16. Waisbren SE, Weipert CM, Walsh RC, Petty CR, Green RC: **Psychosocial Factors Influencing Parental Interest in Genomic Sequencing of Newborns**. *Pediatrics* 2016, **137 Suppl 1**:S30-35.
17. Hayeems RZ, Miller FA, Barg CJ, Bombard Y, Kerr E, Tam K, Carroll JC, Potter BK, Chakraborty P, Davies C *et al*: **Parent Experience With False-Positive Newborn Screening Results for Cystic Fibrosis**. *Pediatrics* 2016, **138**(3).
18. 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**(5):677-682.

Figures

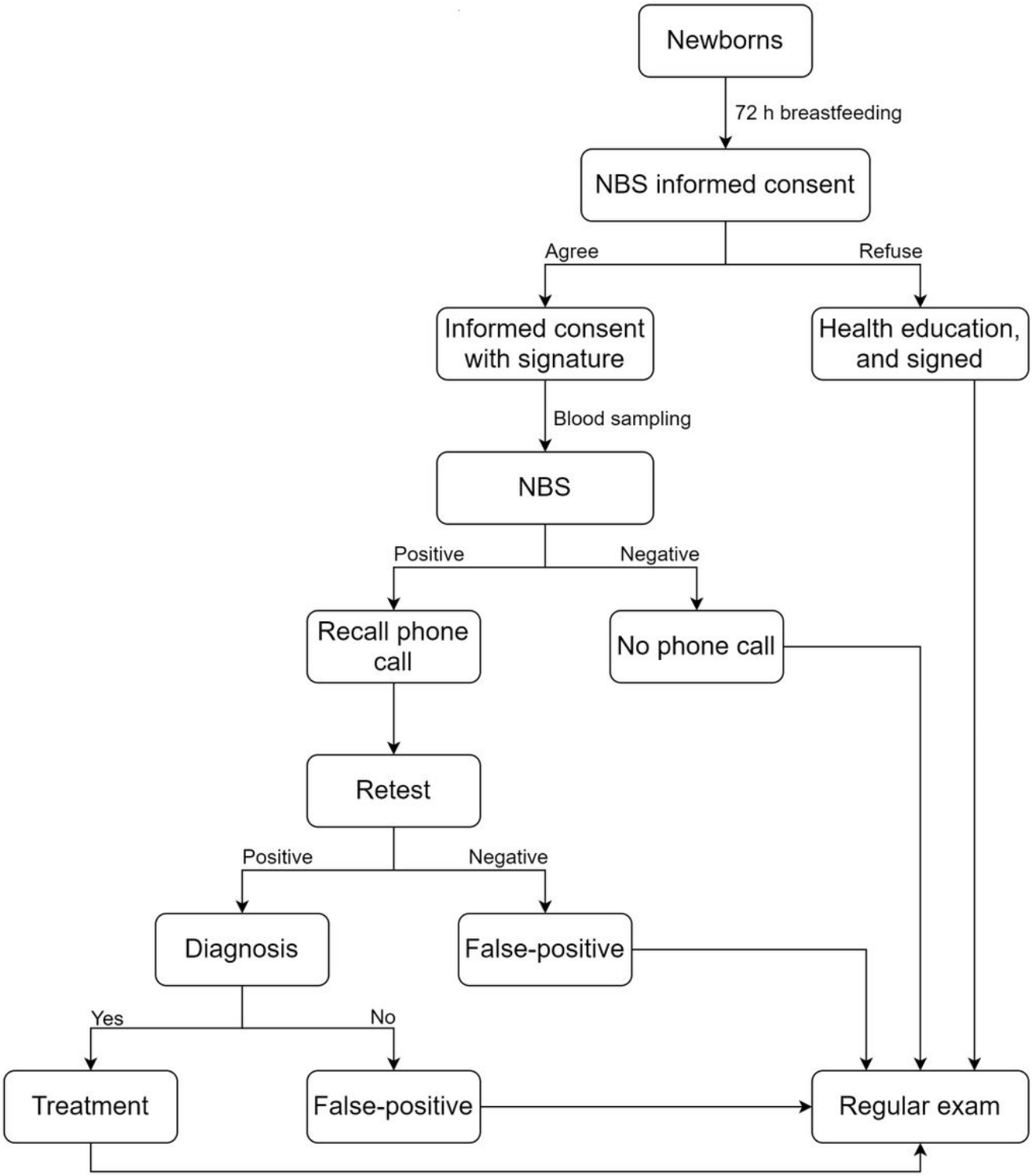

Figure 1

The flowchart of newborn screening in China.

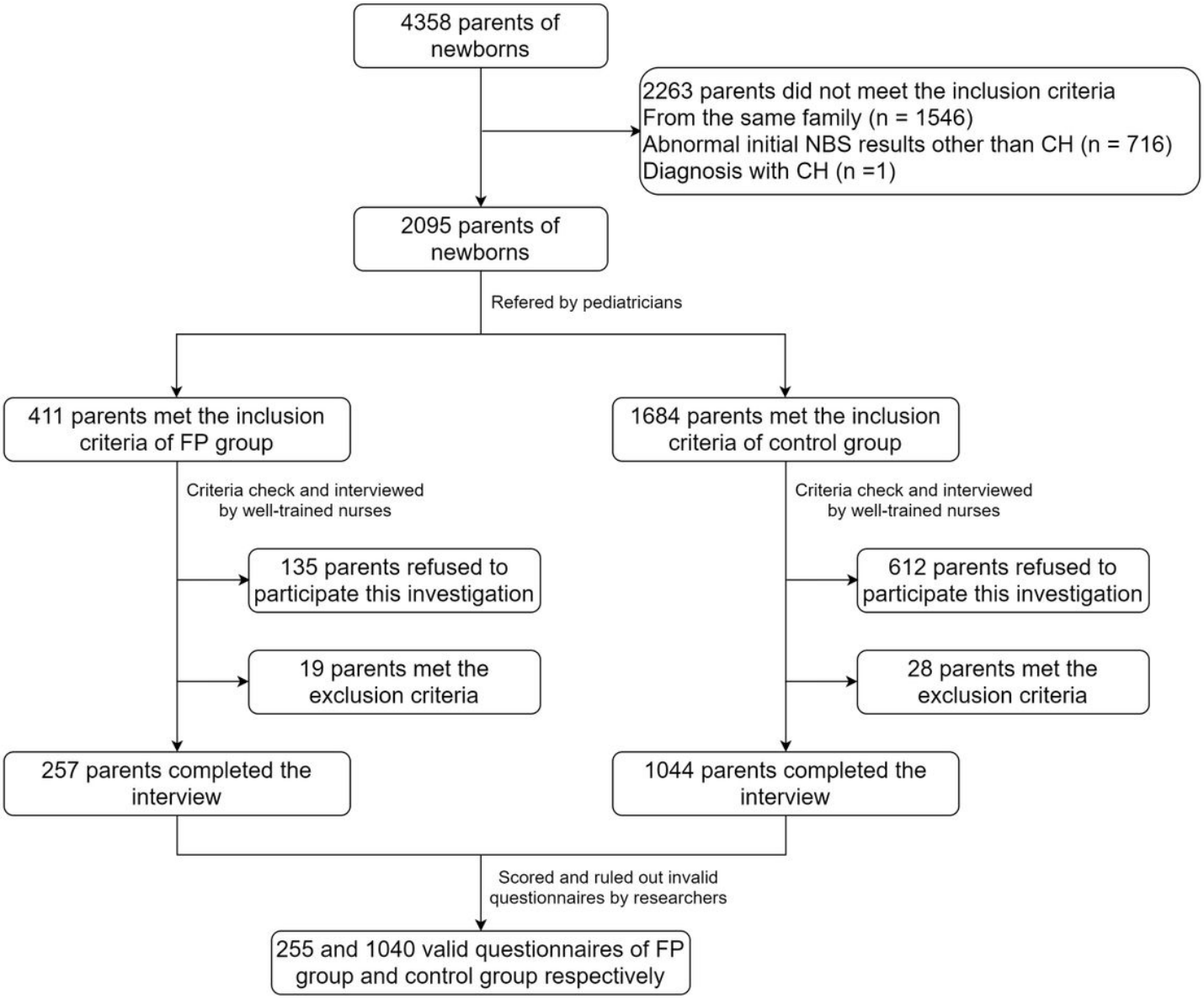

Figure 2

The flowchart of this study.