



GUTHRIE TEST: PERFORMANCE ASSESSMENT OF A NEWBORN SCREENING PROGRAM

TESTE DO PEZINHO: AVALIAÇÃO DE DESEMPENHO DE UM PROGRAMA DE TRIAGEM NEONATAL

TEST DE GUTHRIE: EVALUACIÓN DEL DESEMPEÑO DE UN PROGRAMA DE CRIBADO NEONATAL

Lidyane Rodrigues Oliveira Santos¹, Silvana Santiago da Rocha², Marcia Teles de Oliveira Gouvêia³, Francisco Braz Milanez Oliveira⁴, Anna Karolina Lages de Araujo⁵, Ivalda Silva Rodrigues⁶

ABSTRACT

Objective: to evaluate the performance of the State Newborn Screening Program in the Piauí state. **Methodology:** this is a retrospective study, with quantitative nature, conducted through documental research survey together with the Reference Service for Newborn Screening, in Teresina-PI/ Brazilian Northeast. The subjects were newborns submitted to the Guthrie test by means of the National Health System in 2009. Data were collected from November 2010 to January 2011, after approval of the research project by the Ethics Research Committee from the *Universidade Federal do Piauí* (UFPI), under CAAE nº 0316.0.045.000-10. **Results:** data analysis has revealed advance with regard to the coverage, totaling 96.87%, it was found that 87.67% of the surveyed newborns performed such a test in the first week of life. The diagnosed diseases were: Congenital Hypothyroidism and Phenylketonuria. **Conclusion:** the program has advanced with respect to the coverage. However, the state needs to adapt itself to include other phases of the program and to reach a rate of LB 100% coverage. **Descriptors:** Newborn Screening; Early Diagnosis; Newborn.

RESUMO

Objetivo: avaliar o desempenho do Programa Estadual de Triagem Neonatal no estado do Piauí. **Metodologia:** estudo descritivo, com natureza quantitativa, realizado por meio de levantamento de pesquisa documental junto ao Serviço de Referência em Triagem Neonatal/SRTN, em Teresina-PI/Nordeste do Brasil. Os sujeitos foram os recém-nascidos submetidos ao exame do Teste do pezinho por meio do Sistema Único de Saúde em 2009. Os dados foram coletados no período de novembro de 2010 a janeiro de 2011, depois da aprovação do projeto de pesquisa no Comitê de Ética em Pesquisa da Universidade Federal do Piauí (UFPI), sob CAAE nº 0316.0.045.000-10. **Resultados:** a análise dos dados revelou avanço quanto à cobertura, totalizando 96,87%; verificou-se que 87,67% dos recém-nascidos pesquisados fizeram o teste na primeira semana de vida. As doenças diagnosticadas foram: Hipotireoidismo Congênito e Fenilcetonúria. **Conclusão:** o programa avançou, no que tange à cobertura. No entanto, o estado necessita adequar-se para abranger outras fases do Programa e atingir um índice de 100% de cobertura dos NV. **Descritores:** Triagem Neonatal; Diagnóstico Precoce; Recém-Nascido.

RESUMEN

Objetivo: evaluar el desempeño del Programa Estatal de Cribado Neonatal en el Estado de Piauí. **Metodología:** estudio descriptivo de naturaleza cuantitativa, llevado a cabo mediante encuesta de investigación documental en el Servicio de Referencia en Cribado Neonatal (SRTN), en la ciudad de Teresina, Estado de Piauí, nordeste de Brasil. Los sujetos fueron recién nacidos sometidos al test de Guthrie a través del Sistema Unificado de Salud en 2009. Los datos fueron recogidos en el período de noviembre de 2010 a enero de 2011, posteriormente a la aprobación del proyecto de investigación por el Comité de Ética en la Investigación de la Universidad Federal de Piauí (UFPI) bajo el Certificado Nº 0316.0.045.000-10. **Resultados:** el análisis de los datos reveló adelanto con respecto a la cobertura, con un total de 96,87%. Se verificó que 87,67% de los recién nacidos investigados habían realizado el test en la primera semana de vida. Las enfermedades diagnosticadas fueron: hipotiroidismo congénito y fenilcetonuria. **Conclusión:** el programa ha avanzado con respecto a la cobertura. Sin embargo, el estado tiene que adaptarse para abarcar otras fases del programa y llegar a un índice de 100% de cobertura de los nacidos vivos. **Descriptores:** Cribado Neonatal; Diagnóstico precoz; Recién nacido.

^{1,5,6}Nurses Graduated from the *Universidade Federal do Piauí/UFPI*. Teresina(PI), Brazil. E-mails: lidyanero@yahoo.com.br; karol_lages@hotmail.com; ivaldinha@hotmail.com; ²Nurse, Professor Ph.D in Nursing, Nursing Department/Post-Graduate Program in Nursing, Health Sciences Center, *Universidade Federal do Piauí/UFPI*. Teresina (PI), Brazil. E-mail: silvanasantiago27@gmail.com; ³Professor Master Nursing, Nursing Department, from the Health Sciences Center, *Universidade Federal do Piauí/UFPI*. Teresina (PI), Brazil. E-mail: marcia06@gmail.com; ⁴Nurse, Master's Student, Post-Graduate Program in Nursing, *Universidade Federal do Piauí/UFPI*. Teresina (PI), Brazil. E-mail: braz_cm@hotmail.com

INTRODUCTION

The term “newborn screening” means choosing, separation of a group, refers to tests that can be performed within the first hours of life of the newborn. In Public Health, this is defined as a primary action of screening programs aimed at detecting diseases that can cause great damages to the growth and development of affected children, if diagnosis and treatment are not made in a timely manner. On the other hand, if such a test is made in proper time and manner, it can avoid catastrophic consequences for the child’s development, including death.¹⁻³

The history of the Newborn Screening Program began in 1961, with Dr. Robert Guthrie, medical researcher who developed the method of collecting blood samples on filter-paper, in Jamestown- New York/USA, when researching the Phenylketonuria in children from two hospitals whose blood samples were sent to the laboratory of the Newark State School. In Brazil, its origin dates back to 1976 with the Dr. Benjamin Joseph Schimidti studies, who performed the first tests for the research on the Phenylketonuria in the APAE laboratory at the São Paulo state.⁴ With the creation and implementation of the National Newborn Screening Program - *Programa Nacional de Triagem Neonatal* (PNTN) by Ordinance of the Brazilian Ministry of Health - GM/MS ° 822/2001 -, it was possible to detected, by means of the test at stake, congenital pathologies in the pre-symptomatic phase in all live births, allowing an effective treatment.⁵

The Newborn Screening, commonly called “Guthrie Test”, is a free exam and required by law and, preferably, should be performed between the 3rd and 7th day of the child’s life, extending to the deadline until, at most, the 30th day after birth, thus enabling an early diagnosis and possible treatment in case of confirmation of some pathology. By considering the unequal situation between the federal units, with regard to the implementation and coverage of the screening, the PNTN is organized in phases, so that the states’ adherence to each phase of the program can be conducted when the requirements of the previous phase are fulfilled.⁶

The PNTN has three phases : at the Phase I, the Hypothyroidism and Phenylketonuria tests are performed (PKU); at the Phase II, besides the Phase I tests, the hemoglobinopathies test is included (Sickle Cell Disease), and at the Phase III: Phase I and I tests plus Cystic

Fibrosis test are performed.⁷ In Brazil, 14 states perform the Phase I tests (AC, AL, AM, AP, CE, DF, MT, PA, PB, PI, RN, RR, SE and TO) 10 states already conduct the Phase II tests (BA, ES, GO, MA, MS, PE, RJ, RS, RO and SP) and 3 states conduct even the Phase III tests (SC, PR and MG).⁸

At the state level, it was only at the end of 2004 that the Ministry of Health - *Ministério da Saúde* (MS) has enabled the Piauí state in the State Newborn Screening Program - *Programa Estadual de Triagem Neonatal* (PETN) by accrediting the *Hospital Infantil Lucídio Portela* (HILP) as Reference Service for Newborn Screening - *Serviço de Referência em Triagem Neonatal* (SRTN). In January 2005, the Piauí state started to carry out the test for free by the Unified Health System - *Sistema Único de Saúde* (SUS), and is enabled to perform the screening of Phase I pathologies, Congenital Hypothyroidism and Phenylketonuria. According to data provided by the State Coordination for Newborn Screening from the Health Department of the Piauí State, before the implementation of the aforementioned program, only 8% of live births performed the test.

The collection is held in health centers in the municipalities of the state countryside, and in Teresina city it is performed at the state Maternity, which is a referential in the Piauí state, or in some hospitals/maternity hospitals in peripheral neighbourhoods of the capital. Thus, given the complexity, importance and repercussion of this study, its design was extremely important, in order to assess the performance of the State Newborn Screening Program in the Piauí state and, thus, to contribute to the empowerment of the state in the other PNTN phases.

OBJECTIVE

- To evaluate the performance of the State Newborn Screening Program in the Piauí state.

METHOD

This is a retrospective study, with quantitative nature, conducted through documental research survey together with the Reference Service for Newborn Screening, located in Teresina-PI/ Brazilian Northeast.

The sample size was calculated based on live births in the year 2009 (50.996), of which, 77.14% were screened by the program (39.343), the study population was comprised of all newborns (NB) submitted to the Guthrie test by the SUS in that year. The tool used for data collection was previously elaborated,

filled out by researchers, with information contained in the SRTN databases and in medical charts of patients under treatment. Data were tabulated in the Microsoft Office Excel, and the results were presented in tables. During the statistical analysis, a measure of the rate of association between the study variables was performed.

Data collection was conducted from November 2010 to January 2011, after approval of the Project in the CEP. In accordance with the ethical principles, the privacy of the research subjects was guaranteed, given that the medical chart queries, of cases under treatment, were blinded as the agreement of the institution. This project was registered in Ethics Research Committee - *Comitê de Ética e Pesquisa* (CEP) from the *Universidade Federal do Piauí*

(UFPI), with CAAE nº 0316.0.045.000-10, by fulfilling the requirements of the Regulatory Standards and Guidelines for Researches, ruled by the Resolution 196/96 of the National Health Council.⁹

RESULTS AND DISCUSSION

Since the implementation of the PETN, in 2005, in the Piauí state, there was an increase of more than 100% in the coverage of live births (LB) in comparison to 2009, as presented in Table 1, which shows that from the 50.996 NV in that year, 39.343 of them performed the Guthrie test, with coverage of 77.14%. It was noted a relative decrease of births over the five years, but with a significant increase in the examination conductions.

Table 1. Distribution of the State Newborn Screening Program coverage by the number of live births and examinations performed between 2005 and 2009. Teresina (PI), 2010.

Year	Nº Live births (Lb/Year)	Examinations/Year	% Coverage (Lb/Year)
2005	56.866	21.025	36,97%
2006	55.342	32.103	58,00%
2007	53.214	35.038	65,84%
2008	52.664	35.671	67,73%
2009	50.996	39.343	77,14%

Source: SRTN/PI

In 2009, of 39.343 births, 34.495 (87.7%) underwent the test during the first week of life, while 4.848 (12.3%) newborns were

submitted to the examination with more than 8 days of life, as shown in Table 2.

Table 2. Distribution of the number of days of the newborns during blood sampling performance for screening test in the year 2009. Teresina (PI), 2010.

Month	NB with up to 7 days of life	NB with 8-30 days of life	NB >30 days Of life	Total (nº)
Jan	2.198	322	78	2.598
Feb	2.269	429	80	2.778
Mar	4.692	786	123	5.601
Apr	3.211	322	49	3.582
May	3.077	199	65	3.341
June	3.010	222	69	3.301
July	3.144	266	75	3.485
Aug	2.944	280	75	3.299
Sept	2.666	167	42	2.875
Oct	2.987	346	61	3.394
Nov	2.422	396	66	2.884
Dec	1.875	274	56	2.205
Total	34.495	4.009	839	39.343

Source: SRTN/PI

Before the aforementioned data, it should be noted that 4848 children (10.12%) underwent the screening test after the time recommended by the Ministry of Health, with average rates of 2% of exams conducted after 30 days. These data show that yet a significant portion is at the mercy of a late diagnosis, which disfavors an active search and immediate treatment.

The American Academy of Pediatrics recommends the collecting at the earliest time of the hospital discharge of newborns at term and in good health status and, in no

hypothesis, this may exceed the seventh day of life, since early identification and treatment prevent sequelae, including the severe and irreversible neurological damages, as global developmental delay and deep mental retardation, as in the case of Phenylketonuria.¹⁰

For this purpose, it is of utmost importance having the operation of the Family Health Strategy, in active search of pregnant women for awareness and test performance at the first week of the child's life. Since an inadequate prenatal assistance may directly

influence the health of the mother-child binomial, so it becomes important to know the profile of attended women, as well as the quality of care provided to them during the prenatal period. Hence, the Family Health Program team will have greater opportunity to intervene more effectively in relation to the health promotion of this population, as it prioritizes a working dynamic in the primary care scope.¹¹

As for the adherence of municipalities in the Piauí state to the State Newborn Screening Program, when considering the start of the program, in 2005, it was identified that - in four years - the state coverage has reached 96.87%, through the membership of 217 municipalities that organized themselves according to the pre-established criteria to perform the blood sampling. It should be noted that there are 253 deployed collection units, which shows that there is more than one collection station in some municipalities whose demands are more intense.

It was also analyzed the screening test quality and it was found that only in 2009, 446 newborns (1.13%) were recalled, 240 due to inadequate sample and 206 due to insufficient material. While we are witnessing a small rate, it is known that the puncture collection technique is uncomplicated and affordable and there should be no users recall.

Nonetheless, some special situations require a 2nd collection, i.e., later, as in the case of premature NB, underweight or in critical condition, which may have false negative results in newborn screening for Congenital Hypothyroidism, and it is recommended a new collection in 7-14 days. In the case of blood transfusions, PNTN recommends the (re)collection in 90 days.¹²

24 confirmed cases in the state in 2009 were recorded, which were diagnosed through the Phase-I screening test, from which the data showed a higher incidence of Congenital Hypothyroidism (87.5%) in relation to the Phenylketonuria (PKU) (12.5%).

The Phenylketonuria is a metabolic disorder of recessive autosomal inheritance in which there is deficiency of the phenylalanine hydroxylase enzyme (PH), and it has difficult clinical suspicion, which is largely due to the lack of knowledge on the part of doctors about such a condition, which is often confounded with autism, Angelman Syndrome, hyperactivity disorder with attention deficit, among others.¹³

Just as Phenylketonuria, the Congenital Hypothyroidism, which is characterized by a deficiency in the effective functioning of the

thyroid, although it is treatable, children who have such a disease will live with it throughout life. Nevertheless, professionals should be able to discern whether the condition is temporary or permanent, for beginning the treatment of the confirmed cases.

In principle, there is no a secure method that allow us to differentiate permanent congenital hypothyroidism from the temporary type in the NB, without running the risk of losing precious time. Hence, even though hypothyroidism is temporary, the early initiation of the treatment is crucial to prevent possible sequelae.¹⁴

Thus, the American Academy of Pediatrics and the American Thyroid Association affirm that the treatment initiated up to 15 days of the child's life is able to ensure normal neurological development, even in most severe cases.¹⁵

The treatment provided to patients with Phenylketonuria is nutritional, with a phenylalanine-free formula that they receive from the SUS; furthermore, they perform a follow-up with a multidisciplinary team. For patients with Congenital Hypothyroidism, the treatment is based on medications (through levothyroxine); they receive such a medicinal drug in their hometowns, also from SUS, besides regular monitoring by the SRTN staff.

The impact of the congenital defects in Brazil has progressively increased, rising from fifth to second cause of deaths in children under one year old, between 1980 and 2000, a fact that points out to the need for specific strategies in Health Policy.¹⁶

Nursing plays an utmost and indispensable role in the PNTN, because it interacts with the target audience: the mother and the newborn, since the prenatal period in the Basic Health Units. This professional informs and guides the mother that, after childbirth, the baby will go through a simple and very important examination, which is the "Guthrie Test". So, the future mother will be aware that should require the examination after her child is born.⁴

CONCLUSION

The study allowed us to conduct an actual examination of the State Newborn Screening Program performance in the Piauí state, by enabling addressing the achieved positive points, as well as challenges and difficulties inherent in the advancement. Thus, it is of utmost importance to raise awareness among managers and professionals with regard to

reach the goal of LB 100% coverage, through the implementation of such a test in all municipalities of the state, by facilitating the users' access to the examination. The base is grounded in primary care, in the active search and counseling of pregnant women in prenatal care, by addressing the family members concerning the importance of the screening test, and the share of the multidisciplinary teams is fundamental to hold a more effective approach, thus enabling the early diagnosis and treatment, in order to avoid significant sequelae in the child development.

This study seeks to broaden the viewpoint of professionals, managers and healthcare services' users on the benefits of the newborn screening program, by working in a systematic way in disseminating and expanding, in order to provide a better life quality through an immediate treatment guaranteed by the SUS; besides providing data to facilitate the implementation of actions to promote the dissemination and awareness of managers, professionals and students in the health field, as well as the society to the importance of an integral care in the newborn screening accomplishment.

ACKNOWLEDGEMENT

- Study conducted with support from Brazilian National Council for Scientific and Technological Development/ Institutional Program of Scientific Initiation Scholarships /CNPq PIBIC/UFPI, 2010-2011. Teresina (PI), Brazil

REFERENCES

1. Brasil MS. Manual de Normas Técnicas e Rotinas Operacionais do Programa Nacional de Triagem Neonatal. SAS (MS): Brasília; 2003.
2. Botler J. Triagem Neonatal-o desafio de uma cobertura universal e efetiva. Revista Ciência & Saúde Coletiva,online [Internet]. 2010 May [cited 2010 Mar 15];15(2):493-508. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-81232010000200026
3. Therrell BUS. Newborn screening policy dilemmas for the twenty-first century. Mol Gen Metab online [Internet]. 2001 May [cited 2001 Sept-Oct 20];74(1-2):64-74. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/11592804>
4. Silva MBG; Lacerda MR. Teste do Pezinho: por que coletar na alta hospitalar. Rev Eletrônica Enferm, online [Internet]. 2003 May [cited 2003 Sept 30];5(2):60-4. Available from:
5. Brasil. Secretaria de Atenção a Saúde. Departamento de Atenção Especializada. Manual de Educação em Saúde / Brasília : Editora do MS; 2008.
6. Pereira LB. A triagem neonatal como mecanismo de promoção das capacidades humanas[dissertação]. Brasília(DF), on line [Internet]. 2009 May [cited 2009 Feb 6]. Available from: <http://repositorio.bce.unb.br/handle/10482/4516>
7. Jesus JA de. Doença Falciforme no Brasil. Gaz méd. Bahia on line [Internet]. 2010 May [cited 2010 Sept 22];80 (3):8-9. Available from: www.gmbahia.ufba.br/index.php/gmbahia/article/view/1102/1058
8. Sociedade Brasileira de Triagem Neonatal, Locais de Realização de Exames - Público online [Internet]. 2011 May [cited 2011 May 15]. Available from: http://www.sbtn.org.br/pg_triag_oquee_locexame_publico.htm
9. Ministério da Saúde (BR). Conselho Nacional de Saúde. Resolução Nº 196, de 10 de outubro de 1996. Trata das diretrizes e normas de regulamentação de pesquisas envolvendo seres humanos. Brasília; 1996.
10. Webster D. Quality performance of newborn screening systems: strategies for improvement. J Inher Metab Dis on line [Internet]. 2007 May [cited 2007 Aug 14] 30(4):576-84. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17701286>
11. Uchoa JL, Sales AAR, Joventino ES, Ximenes LB. Indicators of quality of prenatal assistance: pregnant's family's health unit. J Nurs UFPE on line [Internet]. 2010 May [cited 2010 Jan-Mar]4(1):209-17. Available from: <http://www.ufpe.br/revistaenfermagem/index.php/revista/article/view/724>
12. Ministério da Saúde (BR) -Secretaria de Atenção a Saúde. Manual de Normas Técnicas e Rotinas Operacionais do Programa Nacional de Triagem Neonatal; Brasília; 2005.
13. Dan B, Christiaens F, Mewasingh L, De Laet C, Goyens P. Late-treated phenylketonuria mimicking Angelman syndrome. Am J Med Genet on line [Internet]. 2001 May [cited 2001 Oct 23];104: 345-6. Available from: <http://onlinelibrary.wiley.com/doi/10.1002/ajmg.10075/abstract>
14. American Academy of Pediatrics, [Rose SR, Section on Endocrinology and Committee on Genetics, American Thyroid Association,](#)

[Brown RS](#), Public Health Committee *et al*; Update of Newborn Screening and Therapy for Congenital Hypothyroidism. *Pediatrics* on line [Internet]. 2006 May [cited 2006 Jun];117(6):2290-303. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16740880#>

15. Silva LO , Dias MAV, Silva IN, Chagas AJ. Hipotiroidismo congênito transitório: perfil das crianças identificadas no programa estadual de triagem neonatal de Minas Gerais, Arq Bras Endocrinol Metab on line [Internet]. 2005 May [cited 2005 Aug];49(4):521-28. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-27302005000400009

16. Horovitz DDG, Llerena JR JC, Mattos RA. Atenção aos defeitos congênitos no Brasil: panorama atual. Cad Saúde Pública on line [Internet]. 2005 May [cited 2005 Jul-Aug];21(4):1055-64. Available from: www.scielo.br/pdf/csp/v21n4/08.pdf

Submission: 2012/05/14

Accepted: 2013/01/26

Publishing: 2013/03/01

Corresponding Address

Lidyane Rodrigues Oliveira Santos
Avenida Presidente Janio Quadros ,1165 / Bl.
11 / Ap. 202
CEP: 64053-390 – Teresina (PI), Brazil