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DISEASES IDENTIFIED IN NEONATAL SCREENING PERFORMED IN A MUNICIPALITY IN SOUTHERN BRAZIL

DOENÇAS IDENTIFICADAS NA TRIAGEM NEONATAL REALIZADA EM UM MUNICÍPIO O SUL DO BRASIL

ENFERMEDADES IDENTIFICADAS EN EL TRIAJE NEONATAL REALIZADO EM UN MUNICIPIO EN EL SUR DE BRASIL

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ABSTRACT

Objective: to know the proportion of diseases detected through the foot tests developed in a town in southern Brazil. **Method:** quantative, retrospective and descriptive study developed in the Neonatal Screening Center from the municipality in sounthern Brazil. Data were collected from records, digitalized, from foot tests done through the Public Health System, from March 2012 to February 2013. **Results**: of 3256 exams developed, 104 had alterated pattern values, of this 60 tests had hemoglobin compatible with falcemic trace, four were diagnosis of phenylketonuria and nine had compatible alterations with Cystic fibrosis. **Conclusion:** the most incident disease in evaluated exams, sickle cell anemia, is related to ethinic chacacteristics of Black population. Knowing the proportion of the diseases detected helps in the elaboration of the early diagnosis in the neonatal period, making possible the creation of specific health care strategies in the study municipality.

Descriptors: Neonatal Screening; Nursing; Infant, Newborn; Disease; Early Diagnosis.

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RESUMO

Objetivo: conhecer a proporção das doenças detectadas por meio dos testes do pezinho realizados em um município do Sul do Brasil. **Método**: estudo quantitativo, retrospectivo e descritivo, realizado no Centro de Triagem Neonatal de um município do Sul do Brasil. Coletou-se os dados a partir dos registros dos testes do pezinho realizados pelo Sistema Único de Saúde, entre março de 2012 a fevereiro de 2013. **Resultados:** dos 3256 exames realizados, 104 tiveram valores com padrão alterado, destes 60 tinham hemoglobina compatível com traço falcêmico, quatro eram com diagnóstico de fenilcetonúria e nove possuíam alterações compatíveis com a Fibrose Cística. **Conclusão**: a doença mais incidente nos exames avaliados, anemia falciforme, relaciona-se com a característica étnica da população negra. Conhecer a proporção das doenças detectadas auxilia na elaboração do diagnóstico precoce no período neonatal, possibilitando a criação de estratégias específicas de atenção à saúde no município do estudo.

Descritores: Triagem Neonatal; Enfermagem; Recém-nascido; Doença; Diagnóstico precoce.

RESUMEN

Objetivo: conocer la proporción de las enfermedades detectadas por medio de los tests de Guthrie realizados en un municipio del Sur de Brasil. **Metodologia**: estudio cuantitativo, retrospectivo y descriptivo, realizado en el Centro de Triaje Neonatal de um municipio del Sur de Brasil. Los datos se colectaron a partir de los registros de los tests de Guthrie realizados por el Sistema Único de Salud, entre marzo de 2012 a febrero de 2013. **Resultados:** de los 3256 exámenes realizados, 104 tuvieron valores con patrón alterado, de estos 60 teníam hemoglobina compatible con trazo falciforme, cuatro eran con diagnóstico de fenilcetonuria y nueve tenían alteraciones compatibles con la Fibrosis Quística. **Conclusión:** La enfermedad más incidente en los exámenes evaluados, anemia falciforme, se relaciona com la característica étnica de la población negra. Conocer la proporción de las enfermedades detectadas auxilia en la elaboración del diagnóstico precoz en el período neonatal, posibilitando la creación de estrategias específicas de atención a la salud en el municipio del estudio.

Descriptores: Tamizaje Neonatal; Enfermería; Recién Nacido; Enfermedad; Diagnóstico Precoz.

INTRODUCTION

Neonatal screening "is a set of preventive actions, responsible for identifying individuals with metabolic, genetic, enzymatic and endocrinological diseases" aiming at their adequate treatment to avoid sequels and death.[1:11] The National Neonatal Screening Program (PNTN)), created by GM / MS Ordinance Nº 822 of June 6, 2001[2], instituted the population screening to identify disorders and diseases in the newborn, allowing the treatment and continuous monitoring of the individuals to reduce morbidity and mortality and improve the quality of life in the diseases screened (Phenylketonuria,

Congenital Hypothyroidism, Sickle Cell Anemia and other Blood Diseases, Cystic Fibrosis, Biotinidase Deficiency, and Congenital Adrenal Hyperplasia).[1]

The PNTN is divided into four phases. Each phase requires certain criteria and requirements, and its implementation is regulated by Administrative Rule Nº 822 of June 6, 2001, and, as each State meets the requirements of one phase, it progresses to the next. This occurs according to the following division: Phase I: Phenylketonuria and Congenital Hypothyroidism; Phase II: Phenylketonuria, Congenital Hypothyroidism, Sickle Cell Disease and other Blood Diseases; Phase III: Phenylketonuria, Congenital Hypothyroidism, Sickle Cell Disease and other Blood Diseases and Cystic Fibrosis; Phase IV: Phenylketonuria, Congenital Hypothyroidism, Sickle Cell Disease and other Blood Diseases, Cystic Fibrosis, Biotinidase Deficiency and Congenital Adrenal Hyperplasia.[2]

In this study, the data showed is to a transition period from Phase II to Phase III, and the screened diseases were Phenylketonuria, Congenital Hypothyroidism, Sickle Cell Disease and other Blood Diseases and Cystic Fibrosis.

Phenylketonuria is an innate error of inherited metabolism as an autosomal recessive trait and it is caused by a deficiency or absence of the enzyme to the metabolism of the essential amino acid phenylalanine. The phenotype of most children with phenylketonuria is blond hair, blue eyes, and fair skin, due to the low production of melanin.[3] Phenylketonuria is characterized by the overall delay of neuropsychomotor development.[1]

Congenital hypothyroidism (CH) can be defined as a deficiency of thyroid hormones leading to a reduction in metabolic processes. It is one of the main preventable causes of mental retardation and delays in neuropsychomotor development and it can be prevented when diagnosed and treated early.[4]

Sickle cell anemia is an inherited pathology in which hemoglobin assumes a sickle shape, called hemoglobin S (HbS). There may be homozygous individuals who are carriers of sickle cell anemia (Hb SS) and heterozygous (HbAS) known by having a sickle cell trait.[3] They are considered a genetic change more common in the world and more prevalent in the black population.[5] People with sickle cell anemia may present with hemolytic anemia, pain and vaso-occlusive crises, increased susceptibility to infections, progressive renal failure, and stroke.[1]

Cystic fibrosis (CF) is a serious genetic disorder that mainly affects the lungs and exocrine glands[6], which leads to

an obstructive process related to the increase of mucus viscosity.[1] CF is inherited with an autosomal recessive trait with global incidence of 1:4.[3]

The collection of the "babyfoot test", a recommended screening test to identify the described pathologies, is simple and can be performed within the Maternity Unit, in the Basic Health Units and in the Neonatal Screening Centers of the municipalities. The time for collection should preferably not be less than 48 hours nor more than 30 days of life by a qualified professional between the 3rd and 7th day of life. The ideal day is the 5th day of life.[7]

In a search for publications on neonatal screening in Brazil, several studies were conducted that dealt separately with phenylketonuria[8-9], congenital hypothyroidism, and hemoglobinopathies[9], but did not evaluate neonatal screening in an integral way, with all pathologies screened. Therefore, it was noticed that there is a gap in the productions about the evaluation of the neonatal screening, in a complete way, including all the pathologies screened. A study[9] points out the need for the regionalization of neonatal screening analyzes so it is possible to compose disease panels in each State, aiming at developing more cost-effectiveness strategies.

Based on the above, the following guiding question emerged: what diseases were detected in the "babyfoot test" in a Neonatal Screening Center of a municipality in the South of Brazil? Therefore, the following study had to know the proportion of the diseases detected through the heel pick tests performed in a municipality in the South of Brazil.

METHOD

This is a retrospective and descriptive study with a quantitative approach, developed from the consultation of the heel pick results of live newborn, in a Screening Center of a municipality of the South of Rio Grande do Sul. The study local is responsible for receiving all material collected in the municipal network that performs the test by the Unified Health System and collects the "babyfoot test" of SUS patients.

The available scanned records on the neonatal screening tests performed at the Center, between March 2012 and February 2013 were analyzed, totaling 3256 tests. The choice of this period was due to the transition phase between Phase II (which diagnoses Phenylketonuria, Congenital Hypothyroidism, Sickle Cell Disease, and other Blood Diseases) and Phase III (which identifies

Phenylketonuria, Congenital Hypothyroidism, Sickle Cell Disease and other Blood Diseases and Cystic Fibrosis) of the “babyfoot test”.

For the data collection, a form proposed by the researcher of this research was used, containing: child's birth date, gestational age (considering newborns from 20 weeks to 42 weeks), date of collection, days of life at the time of collection of the test, gender, race, municipality, type of feeding; besides registration of the diseases detected.

After approval by the Ethics Committee of the Faculty of Medicine of the Federal University of Pelotas, under the opinion 1040918, CAAE nº 39816214.2.0000.5317 was carried out in the records. The information collected was organized into a database in the ExcelTM program and then processed in an Epi Info ™ 7 statistical program. A descriptive analysis was performed using absolute and relative frequency.

RESULTS

There were 3256 heel pick tests evaluated, an average of 6 days of life at the time of collection, representing 14.68% of the total sample, and another 14.50% of the neonates collected the test on the ideal day, that is, on the fifth day of life. However, it was noted that there were children who took the exam with approximately one-year-old (Table 1).

Analyzing the sociodemographic data, it was identified that 81.20% of the neonates were born at term, that is, with gestational age between 38 and 42 weeks and, another 18.62% was premature (Table 1). The white race prevailed with 75.34% of the total participants, and in the other category, they were considered brown, yellow and indigenous children (10.23%).

The predominant gender was male (50.98%). Regarding the type of feeding on the day of collection, it is noteworthy that 80.49% of the newborns were exclusively breastfed, while 7.80% of the newborns received another type of food, such as artificial milk and parenteral nutrition (Table 1).

Table 1- Data regarding the collection of the examination in newborns assisted from March 2012 to February 2013 (n=3256). Pelotas, 2015.

Data	n(%)
Days of life in the collection#	
1-3	153 (4,70)
4-7	1746 (53,62)
Até 30	1242 (38,15)
31 – 60	84 (2,60)
61 – 90	13 (0,40)
91 – 120	2 (0,06)
121 – 150	3 (0,09)
151 – 180	2 (0,06)
181 – 337	4 (0,12)
Without information*	7 (0,20)
Gestational Age (weeks)	
At term (38 – 42)	2644 (81,20)
Premature (20 – 36)	606 (18,62)
Without information*	6 (0,18)
Type of feeding	
Exclusive breastfeeding	2621 (80,49)
Mixed feeding	372 (11,42)
Other type of food	254 (7,80)
Without information*	9 (0,28)
Gender	
Female	1596 (49,02)
Male	1660 (50,98)
Race	
White	2453 (75,34)
Black	462 (14,19)
Other	333 (10,23)
Without information	8 (0,24)

* Without information corresponds to losses related to the lack of data filling. #The division by days of life enabled to visualize the number of exams collected in the ideal period and the later collection performed, which interferes in the early detection of changes and in the treatment.

There were 103 (3.16%) tests of the total of 3256 with altered standard values, that is, newborns that have some of the pathologies screened (Table 2).

Table 2- Results of pathologies identified in the "babyfoot test" (n=3256). Pelotas, 2015.

Variable	n (%)
Sickle cell anemia and other blood diseases	
AA (Adult Hemoglobin)	4 (0,12)
AF (Blood transfusion)	21 (0,64)
FAC (Trace of Hemoglobinopathy C)	5 (0,15)
FAD (Trace of Hemoglobinopathy D)	1 (0,03)
FAS (Falcimic Trace)	60 (1,84)
FA (Normal Hemoglobin Standard)	3119 (95,79)
Without information∗	46 (1,41)
Phenylketonuria	
Yes	4 (0,12)
No	3218 (98,58)
Without information∗	34 (1,04)
Cystic fibrosis	
yes	8 (0,34)
No	2325 (71,31)
Inexistent in the period	858 (26,38)
Sweat Testing#	64 (1,97)
Hypothyroidism Congenital	
Yes	0
No	3222(98,96)
Without information*	34 (1,04)

*Without information corresponds to losses related to the lack of data filling. In part of the period, the collection of the "babyfoot test" was in Phase II, that does not include the screening for cystic fibrosis. #Test performed for inconclusive results and for late collection (greater than 30 days).

Changes were observed in the hemoglobin of the newborns, enabling to diagnose sickle cell anemia and other blood diseases, and 60 newborns had hemoglobin compatible with sickle cell trait, determined by FAS. For the pathology of Phenylketonuria, 0.12% of the sample, that is, four newborns of 3256 tests were diagnosed with this pathology.

For the diagnosis of Cystic Fibrosis, when analyzing the results of filter papers collected from newborns with less than 30 days of life, there were eight changes compatible with the disease profile, representing a rate of 0.34% of children detected early with cystic fibrosis. In addition, 858 tests did not contemplate the screening test for cystic fibrosis, since in part of the analyzed period the State was not yet in the phase that allowed the test to be performed.

Sixty-four children were invited to perform the Sweat Test due to late collection, with more than 30 days of life or for diagnostic confirmation. 53 of these 64 children performed the sweat test, and 51 of them obtained values within normality, excluding the pathology. In one test, the presence of cystic fibrosis was confirmed and one test had inconclusive values, with no result confirming or excluding the pathology. Regarding the Congenital Hypothyroidism, none of the 3256 children had the disease.

DISCUSSION

Evaluating data from the National Department of Informatics of the Unified Health System (DATASUS)[11] during the analysis period of prenatal records screening, between March 2012 and February 2013, according to the Birth Information System alive, there were 5227 births recorded per occurrence in the study municipality. Comparing the total number of births with the total number of heel pick tests performed in the SUS network (3256), a difference of 1971is observed. It is noteworthy that part of these children may have been referred to private laboratories or health insurance since this network provides a wider range of pathologies diagnosed by this test. On the other hand, another part of these children may have failed to perform the test due to negligence or lack of knowledge of those responsible about the importance of this examination.

It is known that all the children with some changes in their tests are called to perform another collection in order to confirm the diagnosis since some factors can cause changes in the moment of the biochemical analyzes. Consequently, after the confirmation of a pathology, the children are referred to a specialized

service, seeking to carry out the treatment, follow-up and to receive the specific guidelines to each case.

An important point of the research was the predominance of breastfeeding at the time of collection. This indicates that most newborns are receiving breast milk as a source of food, enjoying its benefits. However, health workers are advised to work with mothers to reduce the rate of children receiving mixed breastfeeding.

The child who receives exclusive breast milk acquires protection against several microorganisms by strengthening their immunity. The use of artificial milk, mixed feeding or feeding with artificial milks only facilitates the occurrence of suckling of milk to trachea and lungs, occurrence of frequent otitis and higher chances of developing cavities.[3]

The States with the highest prevalence of sickle-cell anemia are Bahia (1:650), Rio de Janeiro (1:1,200), Pernambuco, Minas Gerais, Maranhão and Goiás (1:1,400). In Rio Grande do Sul, one every 65 births carries the sickle trait, and one every 11,000 births has sickle-cell anemia.[5]

In this study, 60 of the 3256 children who underwent the test had hemoglobin HbS pattern, determining sickle cell trait. It is possible to observe that the municipality of the study shows the proportion of one child with sickle cell trait for each 53.5 screenings. Therefore, the incidence of sickle cell trait is higher in this municipality than in the state of Rio Grande do Sul. This higher incidence may be related to the fact that the municipality has the largest black population (population in which the disease is most frequent) of the state, since according to the census conducted by the Brazilian Institute of Geography and Statistics (IBGE)[12], the black population in the city was almost 16%, totaling more than 50 thousand people.

The dominant hemoglobin pattern in adults is hemoglobin A (HbA) and in newborns, it is F (HbF).[1] The most frequent variants of hemoglobin are S (HbS) and C (HbC), as well as hemoglobin D, E, and Hasharon, with or without clinical significance.[1] However, sickle cell disease is present when the HbS phenotype predominates, even when associated with other variants.[1]

In this study, there was no occurrence of sickle cell disease diagnosed, since the heterozygous for type C blood diseases were identified in five children, and one child had a type D trait. These children did not have a pathology, but a form of screening genetics indicating a probability of having sick children; and when an individual has the trait for the disease, he or she receives genetic counseling about the likelihood of having a

child with the disease. It is known that the type of hemoglobin is transmitted by genetic inheritance, so if a person who carries the sickle trait has children with another who also has the trait, there is a 25% chance of a child being born with sickle cell disease.[13]

In this context, it is necessary to provide genetic counseling and information sharing on what the blood disease trait is and what it can cause, since the child seems healthy and will not have any clinical symptoms of the disease.

Based on the results obtained in the sickle cell anemia and other blood diseases, it was evidenced that no child in the analyzed population was diagnosed with the pathology, only with the presence of trait for the diseases. Even with these results, it is imperative that all children collect the "babyfoot test", so this genetic screening happens.

Four children with adult hemoglobin (AA) and 21 neonates with blood transfusion (AF) results were also identified in the tests. In both cases, the newborn is called for the collection, to re-examine the hemoglobin chains and to exclude or confirm the possibility of hemoglobin-related disease. However, many children do not return to the collection, even knowing the need and the importance of it. This is an alarming fact, since one of the screening exams, sickle-cell anemia, and other blood diseases are not performed, allowing the children with the pathology to be diagnosed only when they begin to have their classic symptoms, and early diagnosis would favor reduction of problems.

In this study, 3256 children were screened for Phenylalanine levels, of which four were diagnosed with Phenylketonuria. These data show a much higher frequency than the national average which was 1:24,310 children screened in 2002, as well as the world average which is 1:12,000[14].

Phenylketonuria can generate several sequels, such as convulsive seizures and progressive loss of brain function, developmental deficit and behavioral disorders. Therefore, early diagnosis and follow-up is necessary, favoring an adequate dietary guidance treatment from an early age.[15] According to the data obtained through the tests carried out in the study municipality, the diagnosis of the disease has an average higher than national and worldwide, presenting a ratio of 1:805 births. This demonstrates that the tests are being performed in an adequate period, since the child is already ingesting phenylalanine, enabling the diagnosis of phenylketonuria. However, it is important to highlight that these results may be an isolated fact, and

further research is needed to evaluate the occurrence of the disease in other periods.

In Brazil, the estimated incidence of CF is 1:10,000 live births, while in Rio Grande do Sul the incidence is higher, between 1:5,000 and 1:8,000 live births.[16] This frequent incidence for the State is justified by the variation of miscegenation and the predominance of Caucasians in the population.

In the municipality of the study, eight children with CF were identified in the tests carried out and registered by the Unified Health System network, being diagnosed early by the "babyfoot test", which allows the disease to be monitored from the first days of life of the newborn, improving its prognosis and quality of life. A case of CF was still diagnosed through the sweat test. This child had already exceeded 30 days of life, when the Immunoreactive Trypsin (IRT)[17] values decrease, interfering with the diagnosis. In this test, the dosage of chlorine and sodium is carried out in the child's body through sweat, allowing the confirmation or not of the disease.

In the analyses, there were 64 children invited to the sweat test. However, only 53 children were examined. In this context, it is important to reduce the number of children who undergo the sweat test due to late collection, because since CF is a disease of great incidence, collecting the "babyfoot test" on the days recommended would allow the early detection of the disease, favoring the treatment and minimizing the health problems of these children. Therefore, it is necessary to intensify the dissemination about the screening, as well as the active search for children who did not attend the examination call, avoiding late diagnoses.

Congenital hypothyroidism has an occurrence of 1:2,000 to 1:4,000 live births, being more frequent in females.[4] However, in this study, no type of hypothyroidism, whether transient or permanent was diagnosed. However, it should be considered that in the analyzed period, cases of CH may have been diagnosed in tests in the private network. Also, there may be children with late CH diagnosed or not diagnosed. Also, there may be children born and registered in the study municipality, but residing in nearby municipalities. These could have performed the "babyfoot test" in the days following the hospital discharge, in their municipalities where they live.

Several factors may be related to the population coverage of neonatal screening, such as socioeconomic and cultural problems, as well as the lack of information about the importance of the test. In this context, nurses have a fundamental role to guide and inform the women in the pregnancy-puerperal cycle

about the examination, clarifying their purpose, since the lack of information negatively influences the performance of the test, compromising the diagnosis and early treatment.[18]

Thus, it is believed to be important to broaden the discussion about the test, emphasizing the ideal period (3rd to 5th day old) and the ideal conditions of collection (such as puncture site, amount of blood needed and adequate filter paper coverage) both for professionals and for the population, aiming to minimize errors and delays in the diagnosis of pathologies. Also, the recording of the results is very important for reliability of the information about "babyfoot test".

It is highlighted that the "babyfoot test" should be collected in the appropriate period, since the delays interfere in the diagnosis and treatment, and may lead to the development of sequels in children. Therefore, it is recommended that the collection of the test be performed in the maternity ward when appropriate, or until the child's 5th day of life.[10] It is important that the primary health care team is attentive to the neonatal screening and presence of changes in results to minimize losses and late diagnoses.[19]

CONCLUSION

The "babyfoot test" is essential for the preparation of the early diagnosis in the neonatal period. It is observed that blood diseases are the most frequent in the pathologies detected in this study, followed by cystic fibrosis and phenylketonuria, enabling to create specific neonatal health care strategies in the study municipality.

The short time period evaluated is highlighted as limitations that may influence in a greater or lesser incidence of a certain pathology. In addition, the lack of access to the private examinations hindered to identify the reliable frequency of the pathologies screened in the municipality. The study took place during a period of exchange of the screening phase since the faster the municipality migrates in phase, the more pathologies can be screened, diagnosed and treated.

It is necessary to elaborate more studies that contemplate the subject of the neonatal screening by the "babyfoot test" to have a more reliable knowledge about the pathologies most frequently detected and the number of neonates diagnosed. Thus, it would be possible to develop more effective public policies in the diagnosis and treatment of pathologies, minimizing the problems due to lack of identification and early treatment.

REFERENCES

1. Ministério da Saúde (Brasil). Triagem neonatal biológica: manual técnico. Brasília, DF: Ministério da Saúde; 2016.
2. Ministério da Saúde (Brasil). Portaria nº 822 de 06 de junho de 2001. Brasília. DF: Ministério da Saúde; 2001.
3. Hockenberry MJ, Wilson D. Wong fundamentos da enfermagem pediátrica. 9ed. Rio de Janeiro: Elsevier; 2014.
4. Frezzato RC, Santos DCC, Goto MMF, Ouro MPC, Santos CTM, Dutra V, et al. Habilidade motora fina e linguagem expressiva em crianças com hipotireoidismo congênito. CoDAS. [Internet]. 2017 [citado em 04 maio 2018]; 29(1):e20160064. Disponível em: http://www.scielo.br/pdf/codas/v29n1/2317-1782-codas-2317-178220172016064.pdf
5. Jesus JA. Doença falciforme no Brasil. Gaz Med Bahia. 2010; 80(3):8-9.
6. Smyth AR, Bhatt J. Once-daily versus multiple-daily dosing with intravenous aminoglycosides for cystic fibrosis. Cochrane Database of Syst Rev. [Internet]. 2014 [citado em 2017 Oct 27]; 20(1): CD002009. Disponível em: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002009.pub5/epdf
7. Souza ABG. Enfermagem neonatal cuidado integral ao recém-nascido. 2ed. Rio de Janeiro: Atheneu; 2014.
8. Ramalho ARO, Ramalho RJR, Oliveira CRP, Magalhães MMGS, Santos EG, Sarmento PMP et al. Evaluation of effectiveness and outcome of PKU screening and management in the State of Sergipe, Brasil. Arq Bras Endocrinol Metab. 2014, 58(1):62-67.
9. Botler J, Camacho LAB, Cruz MM. Phenylketonuria, congenital hypothyroidism and haemoglobinopathies: public health issues for a Brazilian newborn screening program. Cad Saúde Pública. 2012, 28(9):1623-31.
10. Sales RLUB, Soares APC, Moita Neto JM, Costa RS, Rocha SS, Nogueira. Análise de indicadores de qualidade da triagem neonatal sanguínea. Rev Enferm UFPE. [Internet]. 2015 [citado em 04 maio 2018]; 9(2):677-82. Disponível em: https://periodicos.ufpe.br/revistas/revistaenfermagem/article/view/10387/11140
11. Ministério da Saúde (Brasil), Departamento Nacional de Informática do Sistema Único de Saúde. DATASUS [Internet]. Brasília, DF: Ministério da Saúde; [201-] [citado em 29 out 2017]. Disponível em: http://www.datasus.gov.br
12. Instituto Brasileiro de Geografia e Estatística. Censo demográfico de 2000: características da população e dos domicílios: resultados do universo. Rio de Janeiro: IBGE; [200-] [citado em 29 out 2017]. Disponível em: http://www.ibge.gov.br/home/estatistica/populacao/censo2000
13. Ministério da Saúde (Brasil). Doença falciforme: o que se deve saber sobre herança genética. Brasília, DF: Ministério da Saúde; 2014.
14. Nunes AKC, Wachholz RG, Rover MRM, Souza LC. Prevalência de patologias detectadas pela triagem neonatal em Santa Catarina. Arq Bras Endrocrinol Metab. 2013; 57(5):360-7.
15. Santos MP, Haack A. Fenilcetonúria: diagnóstico e tratamento. Comun Ciênc Saúde. 2012; 23(4):361-68.
16. Rizzo LC, Fischer GB, Maróstica PJC, Mocelin HT. Profile of cystic fibrosis in two reference centers in southern Brazil. Rev Assoc Med Bras. 2015; 61(2):150-5.
17. Del Campo IRL, Oliveira TQ, Del Campo LA, Sawamura R, Torres LAGMM, Augustin AE, et al. Manifestações precoces da fibrose cística em paciente prematuro com íleo meconial complexo ao nascimento. Rev Paul Pediatr. 2015; 33(4):241-5.
18. Marqui ABT. Teste do pezinho e o papel da enfermagem: uma reflexão. Rev Enferm Atenção Saúde [Internet]. 2016 [citado em 27 out 2017]; 5(2):96-103. Disponível em: http://seer.uftm.edu.br/revistaeletronica/index.php/enfer/article/view/1605/pdf.
19. Sosnay PR, Farrell P. Challenges in cystic Fibrosis newborn screening and

recommendations for primary care physicians. Pediatrics [Internet]. 2015 [citado em 2017 Oct 27]; 136(6):1181-84. Disponível em: http://pediatrics.aappublications.org/content/early/2015/11/11/peds.2015-3490

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