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EPIDEMIOLOGICAL PROFILE OF CHILDREN WHO UNDERWENT THE GUTHRIE TEST AT A PUBLIC MATERNITY HOSPITAL IN RECIFE/PE, BRAZIL

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ABSTRACT

Objective: To identify the epidemiological profile of children who underwent the Guthrie test at a public maternity hospital in the state of Pernambuco - Brazil, in the period from January/2009 to December/2013.
Methods: Descriptive, exploratory, retrospective study, with quantitative approach. Performed at the Center for Integrated Health Amaury de Medeiros - CISAM - in Recife - Pernambuco/Brazil, surveying data from the logbook of the institution, collecting the amount of visits, tracing an epidemiological profile by gender, incidence of positive cases for examinations carried out by the National Neonatal Screening Program (NNSP). Presented through tables and figure.
Results: Data show 11,269 performed examinations and 446 positive cases for Phenylketonuria, Congenital Hypothyroidism and Sickle Cell Anemia, in which the highest percentage was positive and/or sickle cell traits.
Conclusion: the lack of guidance from professionals about the importance of screening leads to low demand, lack of clarification regarding the test, late diagnosis, thus hidering the initiation of treatment.

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INTRODUCTION

The National Neonatal Screening Program (NNSP), more commonly known in Brazil as the "Guthrie Test", is a public policy which is part of the Department of Specialized Care, which aims at, in addition to identifying the holders of any pathology of the program, performing the active search of positive cases to insert them appropriately into the follow-up by a multidisciplinary team and integral care, starting the treatment quickly to prevent sequels and reduce morbidity and mortality, improving the quality of life (Botler; Camacho; Cruz, 2012; Brazil, 2016). The NNSP was implemented in Brazil in 2001, aiming at a coverage of 100% of newborns. However, due to various problems, such as the difficulty access to the examination, the resistance by parents or guadiansto perform it and the unawareness of the importance of the examination, there is still an insufficient and uneven population coverage, with significant differences between the various regions of the country, becoming factors that lead to no population coverage of neonates (Brazil, 2008; Silva *et al*., 2015). The neonatal screening offers benefits such as the discovery of serious and treatable diseases before the onset of symptoms. Laws have been created to provide coverage of care to the child with some pathology detected through the Guthrie test, which, after identifying patients with congenital these changes, it is possible to allow a proper approach in the first years of life and a genetic counseling, being able to avoid the complications resulting from the pathology or even death, allowing control of the frequency of these diseases (Mendes; Santos; Bringel, 2013; Silva *et al*., 2015).Thus, the neonatal screening is an important tool for diagnosing these diseases, considering that the clinical symptoms may not be early noticed (Brazil, 2016; Barone *et al*., 2013).

The Brazilian states have the Reference Service in Neonatal Screening (RSNS) and various collection centers distributed by municipalities in the state. The technical team that composes the screening functional structure should be qualified and trained for the blood collection, with technical knowledge regarding material storage, complying with the standards necessary for verification of pathologies, as well as provide guidance to parents about the procedure that will be performed and the test purpose. The collection center is responsible for: maintaining records of collections and withdrawal of results; implementation of active search; sending the material to the accredited laboratory, and delivery of results of examinations considered normal, referencing the positive cases for the reference network, ensuring the documentation and recording of information of newborn babies (NB) who went through the screening (Brazil, 2004; Brazil, 2016). The blood sample collection is an examination from the laboratory analysis of some drops of blood withdrawn from the baby's heel and collected on filter paper, recommended between the third and fifth day of life, preferably breastfed for at least 48h.When there are confirmed cases, these are targeted for completion of specific treatment and/or additional investigations in reference services (Brazil, 2016; Brazil, 2004; Kopacek *et al*., 2015).The main conditions that can interfere with the results of the Guthrie test are: (1) there is no need for fasting to perform the test nor restrictions on the use of medicinal products; (2) the screening of Phenylketonuria must be performed at least 48 hours after the birth for blood collection, otherwise there may be a false normal;(3) the prematurity and occurrence of blood transfusion in the NB may influence the test results for sickle cell anemia and hemoglobinopathies, being recommended a collection in the first days of life and another collection after 90 days to confirm the result;(4) the heel should not be too much pressed for the collection, preferably leaving the blood flow without milking, to avoid hemolysis, and (5) completely fill the circles of the filter paper, avoiding overlapping the blood drops (Mendes; Santos; Bringel, 2013; Brazil, 2004; Fontenele *et al*, 2012). Nursing has an important, nontransferable and undisputed participation in the NNSP because it is responsible for disclosure, information, guidance, and completion of the exam, as well as interacting with the target-patient: mother and NB, in case of positive result of the examination. It is also responsible for active search of cases, performing the recalls to confirm the diagnosis and referencing to units for follow-up.In this context, the Nursing professional is a multiplier agent for information and guidelines on preventive health work (Rodrigues; Araújo; Melo, 2010). This study aimed to identify the epidemiological profile of children who underwent the Guthrie test at a public maternity hospital in the city of Recife/Pernambuco - Brazil, in the period from January/2009 to December/2013, characterizing the sample regarding sociodemographic conditions, identifying positive cases for studied pathologies, determining the prevalence of sickle cell anemia, congenital hypothyroidism and phenylketonuria, verifying the referrals of cases identified.

MATERIALS AND METHODS

This is a descriptive, exploratory, retrospective study, with quantitative approach, conducted at the Center for Integrated Health Amaury de Medeiros (CISAM), in the city of Recife, Pernambuco (PE), Brazil. This institution was chosen for being a reference in neonatal screening in the state of PE, as well as for being a public institution that meets the population demand of neonates in extensive territorial area, offering resources for researches through the results files. This study analyzed the profile of patients that underwent the "Guthrie Test" in the period from January/2009 to December/2013, highlighting gender, days of life when performing the examination and the result of the examination, aiming at improving the quality of life of the population studied, and encouraging the examination still in the first week of life. The data of the attended patients were made available through data obtained in the logbook for active search of the "Guthrie Test". The authors surveyed the data in the institution's logbook, collecting the amount of visits and the result of the respective visits. The study included all screenings carried out in the CISAM, in the period from January/2009 to December/2013. There were 11,269 tests performed during this period; however, the sample consisted of 446, which represented the positive exams for: Sickle Cell Anemia (traits and positive), congenital hypothyroidism and phenylketonuria. The results of the examinations were obtained from the sending of the Central Laboratory of Pernambuco (LACEN-PE), with separation of positive cases and/or traits. Data were processed in a computer, in the program Microsoft Office Excel 2007, presented through graphs and tables and analyzed using descriptive statistics, which verified the implementation of the "Guthrie Test" and the outcome "positive and/or trait" for each collection. This research project was submitted to the Research Ethics Committee (REC) of the University Salgado de Oliveira (UNNIVERSO) that involves human being, data were collected after its approval under CAAE: 32288914.0.0000.5289, complying with the resolution of the National Health Council (CNS) 466/12.

Table 1. General amount of services that performed the Guthrie Test at CISAM, in the period from 2009 to 2013. Recife, 2014

Year	Total	(+)	(-)	Sickle Cell Anemia (Traits)	Sickle cel anemia (Positive)	Hypothyroidism	Phenylketonuria
2009	2691	97	2594	96	00	00	01
2010	2854	119	2735	114	01	01	03
2011	3004	116	2888	111	03	02	00
2012	2022	78	1944	74	01	02	01
2013	698	36	662	35	01	00	00

Source: Primary data/CISAM/PE.

Table 2. Demonstrative of prevalence by gender of the Guthrie Test at CISAM, in the period from 2009 to 2013. Recife, 2014

Year	Total	(+)	(-)	Sickle cell anemia (traits)		Sickle cel anemia (positive)		Hypothyroidism		Phenylketonuria	
				M	F	M	F	M	F	M	F
2009	2691	97	2594	54	42	00	01	00	00	01	00
2010	2854	119	2735	50	64	01	00	00	01	01	02
2011	3004	116	2888	63	48	01	02	00	02	00	00
2012	2022	78	1944	37	37	00	01	01	01	00	01
2013	698	36	662	21	14	01	00	00	00	00	00

Source: Primary data/CISAM/PE.

Table 3. Percentage of positive cases of the Guthrie Test at CISAM, in the period from 2009 to 2013. Recife, 2014

Year	Total	(+)	(-)	Sickle cell anemia (traits)	Sickle cel anemia (positive)	Hypothyroidism	Phenylketonuria
2009	2691	97	2594	3.60%	0.03%	0.00%	0.03%
2010	2854	119	2735	3.99%	0.03%	0.10%	0.03%
2011	3004	116	2888	3.69%	0.09%	0.06%	0.00%
2012	2022	78	1944	3.65%	0.04%	0.09%	0.04%
2013	698	36	662	5.01%	0.14%	0.00%	0.00%

Source: Primary data/CISAM/PE.

Table 4. Time of life with positive result of the Guthrie Test at CISAM, in the period from 2009 to 2013. Recife, 2014

Year	Total	03 – 08 days		09 – 14 days		15 – 20 days		21 – 26 days		≥ 27 days	
		M	F	M	F	M	F	M	F	M	F
2009	97	10	05	13	09	16	11	08	06	09	10
2010	119	10	09	15	21	12	15	12	12	08	05
2011	116	14	13	19	10	09	12	13	07	09	10
2012	78	07	05	09	09	11	09	07	10	05	06
2013	36	01	01	10	02	05	03	04	02	02	06
TOTAL		42	33	66	51	53	50	44	77	33	37
GENERAL TOTAL		75		117		103		121		70	

Source: Primary data/CISAM/PE.

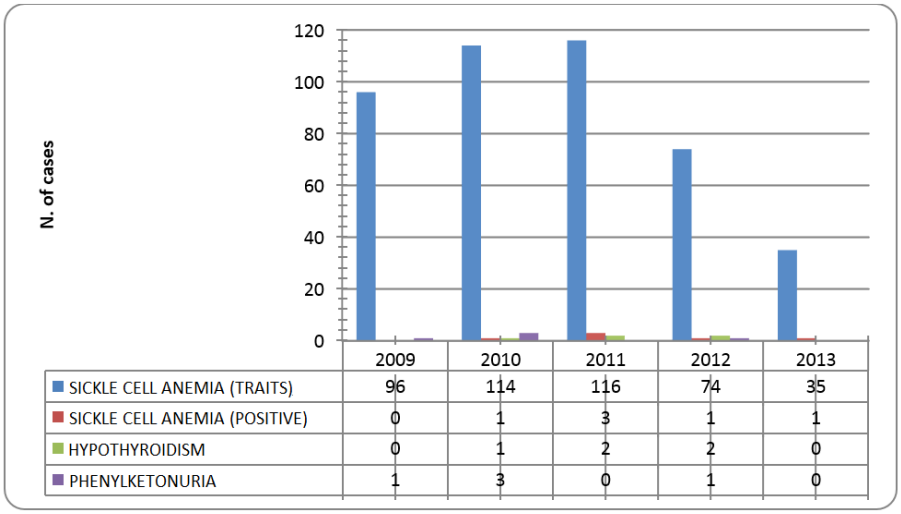
RESULTS

This study allowed identifying the epidemiological profile of children who underwent the Guthrie test during the evaluated period. Table 01 shows the total of services (11,269) conducted according to their respective years, considering as positive the exams with any amendment to be studied. The amount shows the high prevalence of cases of sickle celltraits, compared to cases of congenital hypothyroidism and phenylketonuria. There is also a stability of cases of congenital hypothyroidism and phenylketonuria during the studied years. Regarding the positive cases for the investigated diseases, 446 cases, which show that sickle cell anemia was more prevalent in the years 2010 and 2011, presenting 114 and 116 cases, respectively. The sickle cell trait decreased significantly in the year 2013, and congenital hypothyroidism and phenylketonuriastabilized on zero (Figure 1). However, this was due to the local structural reform in the last year (2013) researched, leading to lack of information for the patients on the service permanence, and with a higher rate of prevalence because the specification of the service demand occurred and wass referenced during the maintenance period. Table 02 shows that, regarding gender, there was a greater incidence of sickle cell anemia in males with resuls for sickle cell traits, and an equity regarding the positive result, remaining a stability regarding gender in this aspect. In relation to congenital hypothyroidism and phenylketonuria, there was a higher incidence in the female gender, highlighting that, in the studied years, only one case of congenital hypothyroidism occurred in males during the whole study period. Observing table 03, there was a stability regarding the rate of incidence of positive cases, with an increase in the last year researched (2013). Due to the local reform, the service could not be maintained, thus ceasing to be offered to a significant portion. Regarding the period to perform examinations, the parents or guardians of those with positive results for the studied diseases do not seek the health service immediately to perform the examination, delaying the screening in comparison to the recommendations of the Ministry of Health. This procedure directly influences the initiation of treatment and/or monitoring when positive. (Table 4). The study showed that, regarding the return to take the result, there is little interest of guardians, even when it is negative. However, among the positive exams that required referencing, all attended the service to withdraw the result due to active search performed by the service (Table 05).

Table 5. Withdrawal of the result ofthe Guthrie Test at CISAM, in the period from 2009 to 2013. Recife, 2014

Year	Total	(+)	Picked up the result		Did not pick up the result		Referenced	
			TOTAL	%	TOTAL	%	TOTAL	%
2009	2691	97	87	89.69%	08	8.24%	02 (HR)	2.06%
2010	2854	119	85	71.43%	28	23.53%	06 (04HR+02HBL)	5.04%
2011	3004	116	77	66.38%	34	29.31%	05 (HBL)	1.68%
2012	2022	78	59	75.64%	15	19.23%	04 (HBL)	5.13%
2013	698	36	26	72.22%	09	25%	01(HBL)	2.77%

*HR – *Hospital da Restauração* (Recovery Hospital)
*HBL – *Hospital Barão de Lucena*(Barão de Lucena Hospital).
Source: Primary data/CISAM/PE.



Source: Primary data/CISAM/PE.

Figure 1. Prevalence of pathologies deteted by Guhtrie Test, in the period from 2009 to 2013. Recife, 2014

DISCUSSION

The objective of the neonatal screening program is to perform the test with speed, allowing the initiation of treatment and preventing sequelae. The delay at any stage of neonatal screening (collection, arrival of the sample in the laboratory, issuing of results, among others) can result in permanent damage to the life of the child affected by the disease and his/her families. The immediate diagnosis and initiation protects the consequences of the disease (Mendes; Santos; Bringel, 2013; Barone *et al*., 2013). The state of Pernambuco is in phase IV in neonatal screening, regulated by the Ministry of Health, which detects pathologies that involve inborn errors of metabolism, endocrine diseases and diseases of genetic inheritance (Kopacek *et al*., 2015). The present study researched about three of the diseases of phase IV. During the survey period, there were six positive cases of Phenylketonuria, which is a hereditary disease, caused by the absence of or decreased activity of a substance produced in the liver, preventing or decreasing the transformation of phenylalanine into tyrosine. It leads to n increased phenylalanine in the blood, which is harmful to the development of the child's brain, causing irreversible mental disability, autistic behavior, seizures and electroencephalographic alterations. The treatment consists of specific diet, with food poor in phenylalanine, complemented by amino acid formula especially prepared for this disease, under strict medical control of the NNSP (Ramalho *et al*., 2014; Kopacek *et al*., 2015; Brazil, 2004). Regarding the cases of Congenital Hypothyroidism, there were five cases. This disease is caused by total or partial failure of thyroid hormones, resulting from various factors, preventing the development of the entire body, including the brain. The consequence of the lack of these hormones is the serious mental disability and impairment in growth and development. It is the most preventable cause of mental retardation. The treatment consists of replacing thyroid hormones under strict medical control so that the child can have a normal growth and development (Palhares *et al*., 2012; Christensen-Adad, 2017; Kopacek *et al*., 2015). The disease with the highest rate of positive cases and traits is the Sickle Cell Anemia, which is the most common genetic disease in Brazil. In this disease, the red blood cells are affected and presented in the form of scythe. This change causes serious difficulties in the circulation and oxygenation of the blood. It does not directly cause mental deficiency, but those affected present complications in the functioning of almost all organs and systems of the body, in addition to greater predisposition to infections, with increased morbidity and mortality. This disease has no cure, but its early diagnosis allows controlling the disease so that the child has quality of life and life expectancy (Brazil, 2004; Silva *et al*., 2015; Wang *et al*., 2015). There is a mistake regarding the disease and the sickle cell trait, being considered a serious problem, found in neonatal screening programs. Health professionals need to provide clarifications to caregivers, offering information about the trait condition, which is not a state of disease and much less an incubated form, which, at any moment, can manifest. Understanding this situation favors relief of anxiety of caregivers when receiving the result (Silva *et al*., 2015). The research showed that, despite the recommendation from the Ministry of Health regarding the ideal period for implementing the screening, the largest amount of collection occurredat days of life far beyond the recommendations (Table 4). A study conducted in Tocantins (Mendes; Santos; Bringel, 2013) showed that the implementation of collection over the indicated periodoccurred

by the exchange of professionals at the collection center, by the permanence of blood samples at the centers and the delay to deliver the results, thus favoring a delay to start the treatment of positive cases. The confirmed cases of Phenylketonuria in the study had low incidence, arriving at some periods to any confirmation of cases. A study carried out in Rio de Janeiro (Botler; Camacho; Cruz, 2012) showed that, in some Brazilian states, the Phenylketonuria rates varied, but were constantly low. The present study showed that the Congenital Hypothyroidism also had a low rate of positive cases. A survey (Oliveira; Ferreira, 2010) showed that the lack of knowledge of care about the Guthrie test favors its low demand and the non-compliance with the treatment. It shows the need for an even greater performance and monitoring of health professionals. In addition to lack of information on the importance of performing the Guthrie test, some conditions can interfere with its results, such as: (1) there is no need for fasting to perform the test nor restrictions on the use of medicinal products; (2) the screening of Phenylketonuria must be performed at least 48 hours after the birth for blood collection, otherwise there may be a false normal;(3) the prematurity and occurrence of blood transfusion in the NB may influence the test results for sickle cell anemia and hemoglobinopathies, being recommended a collection in the first days of life and another collection after 90 days to confirm the result (Brasil, 2004). These diseases have an extremely different outcome when screening occurs within the period and there are early diagnosis and appropriate treatment. It suggests the importance of more pronounced campaigns regarding neonatal screening, favoring the achievement of the goals recommended by the NNSP (Kopacek *et al*., 2015; Oliveira; Ferreira, 2010).

Conclusion

The NNSP deployed in Pernambuco follows the recommendations of the Ministry of Health, and aims to meet 100% of newborns, but some parents/guardians do not seek the screening service to perform the examination, and/or seek the service outside the recommended period for sample collection due to lack of information, thus hindering the beginning of monitoring by the multiprofessional team. The lack of guidance ofthe involved professionals on the importance of screening causes low demand, lack of clarity about the meaning of the test, delay of diagnosis, thus hindering the sense of screening, which is to shorten the days to start the treatment, and the search to withdraw the examination result is still low. The obtained results show the need for the effective participation of the nurse, starting during the prenatal period and ending with the delivery of the exam. As a multiplier agent of information, the nurse must be aware that, during the implementation of the prenatal, the subject needs to be approached, performing guidance for parents regarding the diseases detected by the examination through educational lectures.

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