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# Neonatal screening. A two-year retrospective study in Mexico, from 2019 to 2020

## *Le dépistage néonatal. Une étude rétrospective sur deux ans à Mexico, de 2019 à 2020*

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## ABSTRACT

**Objective.** Congenital diseases are hereditary disorders whose timely detection is vital for early treatment, thus avoiding serious consequences in the future. **Material and methods.** A retrospective study was made of suspected cases of congenital diseases detected through the neonatal screening in a third level hospital of Toluca, Mexico, from the tear 2019 to 2020. **Results.** 30 suspected cases were found between the years 2019-2020, out of a total of 4384 cases, 18 of which were in 2019 and 12 in 2020. Concerning the data collected, the disease with the most prevalence was cystic fibrosis occurring in 14 cases out of 30. **Conclusions.** The most common congenital metabolic disease in our hospital is cystic fibrosis. This study justifies the need to enhance the neonatal diagnosis of metabolic disorders and the need to take the next step with genetic studies to better characterize the affected population.

**Keywords:** Neonatal screening, congenital hypothyroidism, phenylketonuria, congenital adrenal hyperplasia, cystic fibrosis.

## RÉSUMÉ

**Objectif**. Les maladies congénitales sont des troubles héréditaires dont la détection à temps est essentielle pour un traitement précoce, évitant ainsi de graves conséquences dans le futur. **Matériel et méthodes**. Une étude rétrospective a été réalisée sur les cas suspects de maladies congénitales détectés par le dépistage néonatal dans un hôpital de troisième niveau de Toluca, Mexique, de 2019 a 2020. **Résultats.** 30 cas suspects ont été trouvés entre les années 2019-2020, sur un total de 4384 cas, dont 18 en 2019 et 12 en 2020. Concernant les données recueillies, la maladie avec la plus grande prévalence était la mucoviscidose survenant dans 14 cas sur 30. **Conclusion**. La maladie métabolique congénitale la plus fréquente dans notre hôpital est la mucoviscidose. Cette étude justifie la nécessité d'améliorer le diagnostic néonatal des troubles métaboliques et la nécessité de passer à l'étape suivante avec des études génétiques pour mieux caractériser la population touchée.

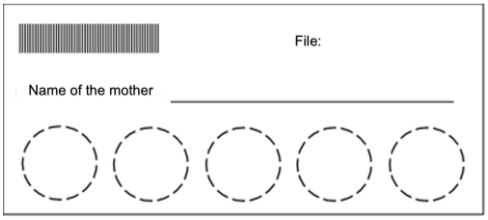
**Mots-clés :** Dépistage néonatal, hypothyroïdie congénitale, phénylcétonurie, hyperplasie congénitale des surrénales, mucoviscidose.

## INTRODUCTION

The beginnings of neonatal screening date back to the 1960s when Robert Guthrie and Ada Susi developed a bacteriological blood test to detect increased levels of phenylalanine, by collecting a few drops of blood that were allowed to dry on a paper special filter [**1**].

Nowadays, the Neonatal Metabolic Screening (NMS) is a multi-test that allows detecting congenital metabolic diseases before they become clinically manifest, leading to an early treatment which improves the prognosis [**2**]. NMS is currently carried out in all countries, through the analysis of blood drops collected on specific filter paper, known as the "Guthrie Card" (**Figure 1**). Another role of the NMS is that it allows a strict follow-up of suspected cases.

**Figure 1.** Guthrie card




In 1973, the NMS was performed for the first time in Mexico, initially only for the detection of galactosemia, homocystinuria, maple syrup urine disease, phenylketonuria and tyrosinemia [2]. In 1995 the neonatal screen was incorporated into the Official Mexican Standard NOM-007-SSA2-1993 "Attention to Women during pregnancy, childbirth, and the puerperium and of the newborn. Criteria and Procedures for the Provision of the Service" [2], and in 2014, a new Official Mexican Standard NOM-034-SSA2-2013" For the Prevention and Control of Birth Defects" was issued, here it was established as mandatory the expanded neonatal screen for the detection of innate errors of metabolism, without specifying the number of diseases that it must diagnose [2].

For its realization first, a blood sample is obtained by puncturing the heel of the newborn from 72 h to 5 days of age, later this sample is placed on the Guthrie card or a specific filter paper [3]. The diseases detected by the NMS in Mexico vary in the different Health Institutions, congenital hypothyroidism being the only compulsory disease in all of them. Specifically, at the Health Institute of the State of Mexico (ISEM), the extended version is used, which mainly detects six diseases: cystic fibrosis, congenital adrenal hyperplasia, congenital

hypothyroidism, galactosemia, glucose 6-phosphate dehydrogenase deficiency and phenylketonuria. The objective of this study was to report the incidence of confirmed cases of these congenital diseases in a public Hospital from Mexico.

## MATERIALS AND METHODS

This was a retrospective study, analyzing the results of the NMS tests of two years, from January 1, 2019 to December 31, 2020, performed at the "Mónica Pretelini Sáenz" Maternal-Perinatal Hospital (HMPMPS), Toluca, Mexico.

The blood samples of the newborns for the neonatal screening were taken with the verbal informed consent of the parents, after explaining its advantages because it is a mandatory action established in Article 6, Section II of the General Health Law and in the Official Mexican Standards NOM-034- SSA2-2013 and NOM-007-SSA2-2016 and were obtained by lancing the heel and collected on the Guthrie card.

The protocol was approved by the Ethics in Research Committee of the HMPMPS (2021-04-725) and informed consent was waived as the medical data was obtained from historical files. Statistical analysis was performed using Excel. The information was treated anonymously, concerning the privacy and confidentiality of the cases.

## RESULTS

In the period of this survey, 30 suspected cases (only cystic fibrosis: 14, congenital adrenal hyperplasia: 10, hypothyroidism: 6 and one newborn positive for cystic fibrosis and phenylketonuria), were found between the years 2019-2020, 18 from 2019 and 12 from 2020 out of a total of 4384 newborns. The main characteristics of the mothers and children are shown in **Table 1**. Regarding the mother's age, cases of cystic fibrosis were found mainly in mothers between 17 and 36 years of age.

**Table 1.** General characteristics of the mothers and newborns

| Variable | Mean ± SD | Minimum | Maximum |
|---|---|---|---|
| **Age of the mothers (years)** | 22.0 ± 5.8 | 14 | 37 |
| **Age of the newborns (days)** | 4.06 ± 0.36 | 3 | 5 |
| **Newborns' weight (gr)** | 3004.7 ± 581.9 | 1690 | 3688 |
| **Newborns' height (cm)** | 49.5 ± 3.1 | 41 | 56 |

**Table 2** shows the quantitative measures of the metabolites used for the congenital diagnosis in the NMS. Interestingly, and talking about weight, a higher incidence of diseases was observed in those children between 3001-3500 gr, being the most frequent cystic fibrosis, followed by congenital adrenal hyperplasia and finally congenital hypothyroidism. Similarly, regarding height, it was seen that most congenital metabolic diseases were in children with a height measure between 46 and 50 cm, leading the cases congenital adrenal hyperplasia, followed by cystic fibrosis, including one case with both diseases.

Regarding the age of the newborn at the time of taking the neonatal screen, in 26 cases it was taken at 4 days of birth, 3 cases at 5 days, and 1 case at 3 days, which indicates that the sample was taken within the normal time range. Concerning the sex of the newborns in the full population, 16 cases were of men and 14 cases of women.

**Table 2.** Mean values of the metabolites in the suspected cases.

| Measure | N and gender | Mean ± SD | Minimum | Maximun |
|---|---|---|---|---|
| **Congenital adrenal hyperplasia (17-hydroxyprogesterone) (ng/dL)** | (N = 10) Men: 8 / Women: 2 | 31.5 ± 40.2 | 129.21 | 2.62 |
| **Cystic fibrosis (trypsin) (ng/mL)** | (N = 14) Men: 6 / Women: 8 | 60.84 ± 45.39 | 173.37 | 5.09 |
| **Hypothyroidism (TSH) (IU/L)** | (N = 6) Men: 2 / Women: 4 | 16.0 ± 52.9 | 283.45 | 0.34 |
| **Phenylketonuria (phenylalanine) (ng/mL)** | (N = 1) Men: 0 / Women: 1 | 79.83 ± 48.08 | 161.74 | 1.07 |

## DISCUSSION

There are about 206 countries worldwide, each one varies in geography, demography, culture, and health system, this diversity also applies to the performance of metabolic screening, which can include the detection of up to 50 diseases. Depending on the region, there are different parameters concerning the sieve, for this work it will be divided into 5 world regions:

- North America: By law, more than 32 diseases are detected. It is intended that the detection is within the first 48 hours and that the results are reported as soon as possible [4].
- Latin America: Neonatal screening has been carried out for 30 years, currently it is reported that up to 70% of newborns are included. The use of expanded neonatal screening has been implemented. Almost all of the countries in this region perform screening for congenital hypothyroidism, 14 for

phenylketonuria, 12 for congenital adrenal hyperplasia, and cystic fibrosis, and 8 for galactosemia [5].

● Europe: There is no consensus about which diseases should be included in neonatal screening, each country individualizes the number of tests to be carried out; the current state of neonatal screening programs in southeast Europe is highly variable and is still underdeveloped or even non-existent in some of the countries [4].

● The Middle East and North Africa: As of 2007, only four countries perform neonatal screening, being the cause of the Marrakech Declaration, which establishes that all countries belonging to this must screen for at least 1 disease [4].

● Asia-Pacific: Only Australia, New Zealand, and Taiwan rely on expanded metabolic screening, relative to India, even though it is one of the countries with the most births in the world, the use of neonatal screening is not a mandatory policy [4].

As a common denominator, it can be found that in countries where there is a poor economy, poor health education, lack of government support, early hospital discharges, and a large number of births, there is a deficit in neonatal screening.

In relation to hypothyroidism, a study carried out in China showed a prevalence of one case in every 3,009 newborns for congenital hypothyroidism [6]. Another study in Latvia, showed an incidence of one in 6,450 newborns with congenital hypothyroidism [7]. In our hospital the incidence was 1 in 730 newborns.

About genetic studies of cystic fibrosis, in Denmark, where 126,338 newborns were analyzed and 4,730 samples were evaluated to detect mutations in the gene *CFTR*, 22 were confirmed to have a diagnosis of cystic fibrosis, four had a known *CFTR* allele, and one of them later was found to carry two *CFTR* variants [8]. Surprisingly, the disease detected using the NMS at the HMPMPS with the highest incidence was cystic fibrosis 1 in 313. This turned out to be a finding since the most commonly detected worldwide congenital disease is hypothyroidism.

In other countries, a higher incidence of cases of other neonatal screening diseases have been found, in Iran between 2015 and 2017 they found three cases of phenylketonuria out of 20,893 (1 in 6964) births, taking into account the tests carried out for the study as part of the phenylketonuria screening program from 2012 to 2015 [9]. An analysis that was carried out from several previous studies from Arab countries, Turkey and Iran, showed that the general prevalence of cases of phenylketonuria was from 0.0198% to 0.0250% [10]. The phenylketonuria incidence in Toluca was of 1 in 4384 newborns. As far as we could investigate, it was found only one reprinted case in the literature with a report of phenylketonuria and cystic fibrosis in the same newborn [11].

In a study conducted in Cuba from January 2005 to December 2010, 621,303 newborns were examined and 39 cases of congenital adrenal hyperplasia were detected [12]. In another study conducted in Brazil in 2014, a total of 159,415 children were examined. In that country, the apparent incidence of the classic variant of the disease was 1: 9,963, according to initial diagnoses after the neonatal screening. During the follow-up period, eight of the 16 children initially diagnosed with congenital adrenal hyperplasia were reclassified as unaffected, resulting in a revised incidence of 1: 19,927. The false-positive rate was 0.31% and the positive predictive value was 2.1%. Sensitivity and specificity were 100% and 99.7%, respectively [13].

By contrast, in this survey, for unknown reasons the incidence was much higher 1 in 438 newborns analyzed.

A study, published an incidence of 33 cases positive for hypergalactosemia in samples collected from 1,123,909 newborns from a neonatology department (years 1982 to 2015) [14], revealing the importance of neonatal screening for the detection and subsequent classification of the condition to treat the underlying cause [15, 16]. The absence of positive cases of this congenital disease in our survey seems to be partially attributed to the relative low number of studies performed in two years.

Glucose-6-phosphatase deficiency was not confirmed in any patient and surely due to its low incidence of 1 in 100,000 births [17], being that in two years we barely carry 0.04% of newborns of the necessary target to detect a case.

Thanks to the comparison of the above-mentioned studies, it could be noted that depending on the country, different congenital diseases are found depending on the complexity of the NMS that is practiced in each of them.

## CONCLUSION

The most common congenital metabolic disease in our hospital is cystic fibrosis and the incidence of this disease as well as those of congenital adrenal hyperplasia and hypothyroidism are higher than that reported in other countries, for which it is justified the need to enhance the NMS national program and the need to take the next step with genetic studies to better characterize the affected population.

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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