Advances in Medicine and Engineering Interdisciplinary Research, 2025, Volume 3, Issue 2
DOI: 10.32629/ameir.v3i2.3737
ISSN Online: 2972-3825
ISSN Print: 2972-3833

Newborn Screening in Colombia: The Experience of a Private Program in Bogotá

Jaime E. Bernal[1, 2*], Martha Lucía Tamayo[3], Ignacio Briceño[4], Escilda Benavides[1]

1. Universidad del Sinú, Colombia.
2. Pregen, Colombia.
3. Pontificia Universidad Javeriana, Colombia.
4. Universidad de la Sabana, Colombia.
*Corresponding author. Email address: jebernal@gmail.com

Abstract: Introduction: The first neonatal screening program in Colombia - PREGEN - was set up in the medical private sector of Bogotá in 1988. We report the results from recent years that, given the scarcity of similar information in our country, may help estimate the frequency of the evaluated neonatal disorders and which ones should be included in the neonatal screening programs in our country. Objective: To describe the results of PREGEN's newborn screening program between 2006 and 2019. Materials and methods: We analyzed databases and other informative documents preserved in PREGEN from the 2006-2019 period. Results: One in every 164 newborns screened in our program had an abnormal hemoglobin variant, and one in every 194 carried some hemoglobin S variant. Glucose-6-phosphate dehydrogenase deficiency and congenital hypothyroidism are next as the more common disorders. Conclusions: Abnormal hemoglobin causes the most frequent monogenic disorder in the world. Glucose-6-phosphate dehydrogenase deficiency is the most common enzymopathy affecting nearly 400 million individuals worldwide. Since both disorders are more common in people of African descent and confer some resistance to malaria, we believe that screening for both disorders may be more relevant in the areas with African ancestry in our country.

Key words: neonatal screening; infant newborn; hemoglobins; congenital hypothyroidism; Colombia

1. Introduction

The term "newborn screening" refers to any type of test administered to newborns to detect those who may develop a disease and thus perform the diagnostic tests required to confirm or rule out the case. A newborn screening program includes an adequate laboratory to perform the required tests on biological samples taken in the first hours or days of a newborn's life. The samples are processed in the shortest possible time by qualified personnel who, in addition to sample collection, are responsible for laboratory analysis, follow-up, and timely treatment of patients.

Newborn screening has been useful in reducing neonatal and infant morbidity and mortality. In less than 50 years, screening methodology has evolved from a small blood or urine sample with relatively simple biochemical analyses to more sophisticated laboratory work that includes next-generation genomic sequencing for the detection of multiple conditions. For this reason, consensus is needed on the laboratory methods to be used and the recommended diseases for screening [1, 2]. A previous communication reported results of neonatal hearing screening using otoacoustic emissions [3].

In Colombia, the first neonatal screening program, called Prevention and Genetics (PREGEN), began operating in the private sector in Bogotá on February 19, 1988. This article presents the results obtained between 2006 and 2019. Given the lack of such studies in the country, these results can be used to estimate the frequency of congenital genetic disorders and thus determine which of them should be subject to neonatal screening in Colombia.

2. Materials and Methods

PREGEN is a private, voluntary program offered to parents of newborns at various clinics in Bogotá. From 2006 to 2019, PREGEN collected newborn samples from the Santafé Foundation, Country, Palermo, de la Mujer, Marly, and La Colina clinics and processed several of them (with the exception of those from the Country clinic) to assess the neonatal thyroid-stimulating hormone (TSH), as required by law. PREGEN maintains a database, updated monthly, that records the total number of patients screened by each test and those who tested positive once the diagnosis was confirmed. Since not all tests were implemented at the same time (mainly due to the commercial availability of reagents), the number of newborns screened between 2006 and 2019 varies from year to year (Table 1).

Table 1. Number of newborns screened

Disease or technique	Screened newborns (n)
Hemoglobinopathies	40,182
Congenital hypothyroidism	129,210
Biotinidase deficiency	30,834
Galactosemia	30,608
Congenital adrenal hyperplasia	30,298
Cystic fibrosis	10,074
Glucose-6-phosphate dehydrogenase deficiency	8,926
Phenylketonuria	2,422
Tandem mass spectrometry	13,714
Total	296,268

Hemoglobinopathies were assessed by high-performance liquid chromatography (HPLC) using the GeneSys2™ instrument (Trinity Biotech Assay). Tests for cystic fibrosis, galactosemia, phenylketonuria, congenital hypothyroidism, congenital adrenal hyperplasia, biotinidase deficiency, and glucose-6-phosphate dehydrogenase (G6PD) deficiency were performed using the Delfia™ enzyme immunoassay analyzer (Perkin Elmer).

Internal controls for the tests are samples with known values provided with the reagents and run concurrently with patient samples. External controls are performed by several entities (Table 2).

Table 2. Entities that perform external quality controls

Entity	Proof	Frequency	Samples analyzed
National Institute of Health	TSH	Four per year	Two batches per shipment, with six samples in each batch.
Department of Health (indirect oversight) Atlanta CDC-PT Unassessed control (measures reproducibility of all tests)	TSH	Monthly	50 samples per month.
	TSH	Four per year	Five samples per test.

Entity	Proof	Frequency	Samples analyzed
	17OHP		
	GALT BTD G6PD IRT PKU, on hold		
Atlanta CDC, quality control (assessed control, measures accuracy)	TSH 17OHP	Four per year	15 samples per test
External Quality Assessment Program of the Argentine Biochemical Foundation	TSH	Four per year	Two batches per shipment

Note: TSH: thyroid-stimulating hormone; 17OHP: 17-hydroxyprogesterone; GALT: galactose-1-phosphate uridyltransferase; G6PD: glucose-6-phosphate dehydrogenase; IRT: immunoreactive human trypsinogen for cystic fibrosis; PKU: Guthrie test for phenylketonuria.

3. Results

Among the 40,182 newborns screened for hemoglobinopathies, 245 were found to have abnormal hemoglobins, 194 with hemoglobin S, followed by those with hemoglobin C (Table 3). In other words, it is estimated that one in every 164 newborns screened in Bogotá by PREGEN had an abnormal hemoglobin variant, and one in every 194 was a carrier of hemoglobin S.

Table 3. Cases of abnormal hemoglobins detected

Hemoglobinopathies	Detected cases (N = 40,182)	Frequency (n)
HBS	194	1 : 207
HBC	34	1 : 1,181
HBE	2	1 : 20,091
HB Barts	3	1 : 13,394
Chain variant A	1	1 : 40,182
Chain variant B	10	1 : 4,018
Chain variant D	1	1 : 40,182
Total	245	1 : 164

Table 4 shows the number of cases detected and the total number of patients screened for each of the seven tests. It is noted that G6PD deficiency and congenital hypothyroidism were the most frequently detected disorders in this group, 1 : 2,231 for G6PD and 1 : 3,915 for hypothyroidism. The results of the cases analyzed by tandem mass spectrometry are shown in Table 5. Eight cases were detected among 13,714 newborns screened, indicating that this method detects disorders in approximately 0.06% of the individuals tested. The most frequent disorders were maple syrup urine disease and methylmalonic acidemia.

Table 4. Cases detected of other disorders

Analyte	Detected cases (n)	Frequency (n)
TSH	33 (129,210)	1 : 3,915
Biotinidasa	1 (30,834)	1 : 30,834
17OHP	1 (30,298)	1 : 30,298
GALT	1 (30,608)	1 : 30,608
G6PD	4 (8,926)	1 : 2,231
IRT	0 (10,074)	
PKU	0 (2,422)	

Note: TSH: thyroid-stimulating hormone; 17OHP: 17-hydroxyprogesterone; GALT: galactose-1-phosphate uridyltransferase; G6PD: glucose-6-phosphate dehydrogenase; IRT: human immunoreactive trypsinogen for cystic fibrosis; PKU: phenylketonuria.

Table 5. Cases detected by tandem mass spectrometry

Tandem mass spectrometry	Detected cases (N = 13,714)	Frequency (n)
Urine with a maple syrup odor	3	1 : 4,571
Methylmalonic acidemia	2	1 : 6,857
Phenylketonuria	1	1 : 13,714
Carnitine deficiency	1	1 : 13,714
Hypermethioninemia	1	1 : 13,714

Finally, Table 6 records the number of repeats performed for the various laboratory tests for various reasons. In general, the frequency of these repeats is low, equal to or less than 1%. Hemoglobin and phenylketonuria tests stand out as the most frequent.

Table 6. Number of repeats required for confirmation of each test

Entity	Repetitions/Total screenings (%)	
Congenital Hypothyroidism	253/129,210	(0.20)
Hemoglobinopathies	334/40,182	(0.83)
Biotinidase Deficiency	136/30,834	(0.44)
Congenital Adrenal Hyperplasia	48/30,298	(0.16)
Galactosemia	89/30,608	(0.29)
Glucose-6-Phosphate Dehydrogenase Deficiency	51/8,926	(0.57)
Cystic Fibrosis	13/10,074	(0.13)
Phenylketonuria	24/2,422	(1.00)

4. Discussion

The first thing that stands out among the 296,268 screenings in this study is that the most frequently found disorders were abnormal hemoglobins (1 : 164), followed by G6PD deficiency (1 : 2,231) and congenital hypothyroidism (1 : 3,915). Two other entities have frequencies less than 1 : 10,000: maple syrup urine disease (1 : 4,571) and methylmalonic acidemia (1 : 6,857); other disorders have a frequency higher than 1 : 13,000, such as phenylketonuria, carnitine deficiency, and hypermethioninemia. The remaining disorders evaluated (biotinidase deficiency, congenital adrenal hyperplasia, and galactosemia) occur in approximately one in every 30,000 newborns.

Hemoglobinopathies are the most common monogenic disorders worldwide, [4] which is confirmed in this study, as it was the most frequent finding among all those studied. G6PD deficiency is an X-linked hereditary predisposition to hemolysis due to a mutation in the gene that codes for the enzyme. It is estimated that nearly 400 million people are affected, making it the most common enzymopathy in the world. [5] Hemoglobinopathies and G6PD deficiency are more common in populations of African origin and confer some degree of resistance to malaria. [6] Bogotá is not a malaria transmission area, and only 1.4% of the population (of 7.59 million in 2019) defined themselves as being of African origin. [7] Therefore, screening for both disorders is expected to have a greater medical and social impact in lowlands and coastal areas where the malaria vector exists and where the majority of Colombians of African descent live. In summary, this study highlights the importance of a comprehensive newborn screening program and the value of extending it to the entire country, especially in a country like Colombia where, between 1998 and 2019, a 32.6% increase in the number of births was observed, going from 140,120 in 1998 to 185,792 in 2019. The Bogotá registry showed that there were 30,552 births per year.

A good screening program is characterized not only by the quality of the laboratory and the inclusion of important diseases for that region, but also by the follow-up of the newborn and their family. Therefore, it is necessary to maintain an excellent sample collection program, adequate processing speed, quality results, and, above all, qualified medical personnel responsible for monitoring and seeking timely treatment for babies with any abnormalities.

It is noteworthy that, in the cohort analyzed in Bogotá, the most frequent disorder was hemoglobinopathies (1 : 164), followed by G6PD deficiency (1 : 2,231), and, in third place, congenital hypothyroidism (1 : 3,915). Other less frequent disorders were detected, but require equal attention. The classic criteria for the inclusion of diseases in massive neonatal screening programs should be taken into account - which consider ethical, social and financial elements [8], as well as the frequency of repetitions, which affects the total cost of the tests, and the growing availability of laboratory techniques on the market [9]. For comparative purposes, references from two previous studies in Colombia are included [10, 11].

Acknowledgments

Ministry of Science, Technology, and Innovation, Project No. CTR 941 of 2019.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

References

[1] Therrell BL, Padilla CD, Loeber JG, Kneisser I, Saadallah A, Borrajo GJ, et al. Current status of newborn screening worldwide. Semin Perinatol. 2015;39:171-87. https://doi.org/10.1053/j.semperi.2015.03.002

[2] Ulm E, Feero WG, Dineen R, Charrow J, Wicklund C. Genetics professionals' opinions of whole-genome sequencing in the newborn period. J Genet Couns. 2015;24:452-63. https://doi.org/10.1007/s10897-014-9779-3

[3] Rojas JA, Bernal JE, García MA, Zarante I, Ramírez N, Bernal C, et al. Transient evoked oto-acoustic emission screening in newborns in Bogotá, Colombia: A retrospective study. Int J Pediatr Otorhinolaryngol. 2014;78:1752-5.

https://doi.org/10.1016/j.ijporl.2014.08.004

[4] Goonasekera HW, Paththinige CS, Dissanayake VHW. Population screening for hemoglobinopathies. Ann Rev Genomics Hum Genet. 2018;19:355-80. https://doi.org/10.1146/annurev-genom-091416-035451

[5] Joseph R, Ho LY, Gomez JM, Rajdurai VS, Sivasankaran S, Yip YY. Mass newborn screening for glucose-6-phosphate dehydrogenase deficiency in Singapore. Southeast Asian J Trop Med Public Health. 1999;30(Suppl.2):70-1.

[6] Cappellini MD, Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. Lancet. 2008;371:64-74. https://doi.org/10.1016/S0140-6736(08)60073-2

[7] Dirección Equidad y Políticas Poblacionales. Población afrocolombiana en el Distrito Capital. Línea de base. Fecha de consulta: 14 de agosto de 2022. Disponible en: https://www.sdp.gov.co/sites/default/files/2011_linea base_bta.pdf

[8] Levy PA. An overview of newborn screening. J Dev Behav Pediatr. 2010;31:622-31 https://doi.org/10.1097/DBP.0b013e3181eedf01

[9] Bermúdez AJ, Robayo DB, González N, Moreno L. Tamizaje neonatal y enfermedades raras. Del test de Guthrie a la espectrometría de masas. Pediatr. 2021;54:28-35. https://doi.org/10.14295/rp.v54i1.173

[10] Unigarro MF, Forero C, Cespedes C. Neuropsychological and physical development of patients diagnosed with congenital hypothyroidism at the San Ignacio University Hospital between 2001 and 2017. Biomédica. 2022;42:144-53. https://doi.org/10.7705/biomedica.6334

[11] Alvear CC, Barboza M, Viola M, Moneriz C, Araque LM. Pilot study of hemoglobinopathies in newborns of the Rafael Calvo maternity clinic of Cartagena, Colombia. Colomb Med (Cali). 2012;43:196-9.

Author Contributions

Jaime E. Bernal: design and data analysis. Martha Lucía Tamayo, Ignacio Briceño, and Escilda Benavides: data analysis and interpretation. All authors participated in writing the manuscript.