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The National Recoding of Orphan Diseases: A Proposal Directed to Health Care

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Abstract:	Introduction: The Asian continent in 1972 was the first to recognize orphan diseases, followed by Europe and later America. In 2010 Colombia since the 1392 law, interdisciplinary work has been noted, however, it is not enough for global knowledge. Objective: To carry out a prevalence analysis, using databases that are freely accessible to the general public, comparing them with the reports made by the entities in charge of the management of the data for the capture, diagnosis and management of orphan diseases in Colombia. Materials and methods: a cross-sectional study was carried out using data cubes The Comprehensive Social Protection Information System (SISPRO) and the microdata of the National Administrative Department of Statistics (DANE), prevalences are estimated, a heat map and a Regression are performed Simple and multiple Poisson with robust variance, adjusted for sex, age, life cycle and region. Results: Information was collected from 2015 to 2018. 3014555 were people treated for one of the 319 diagnoses chosen. The most frequent disease was Viral Warts (14.4%). in females (58.9%), Bogotá (28%) and the Andean region (71%) had the highest. There is a 2.03 times chance for an older adult to have an orphan disease. The highest mortality rate was in the Andean region (0.12%). Discussion: The data obtained in this study differ from those published by the control entities. Conclusions: Quantitative and mixed research should be promoted, as well as a recoding of the diagnoses identified as orphan disease.

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Declarations

This research was financed with the authors' own resources.

The authors declare no conflicts of interest

The information contained in this article is publicly accessible both regionally and nationally in Colombia and corresponds to the national archives.

The software used here has an active license.

Lilian Peña as main author contributed the total research and the submitted manuscript; Alexandra Porras corrected and corroborated the data and statistical tables and Alejandro Rico corrected and corroborated the steps and sources of the investigation.

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Abstract

Introduction: The Asian continent in 1972 was the first to recognize orphan diseases, followed by Europe and later America. In 2010 Colombia since the 1392 law, interdisciplinary work has been noted, however, it is not enough for global knowledge.

Objective: To carry out a prevalence analysis, using databases that are freely accessible to the general public, comparing them with the reports made by the entities in charge of the management of the data for the capture, diagnosis and management of orphan diseases in Colombia.

Materials and methods: a cross-sectional study was carried out using data cubes The Comprehensive Social Protection Information System (SISPRO) and the microdata of the National Administrative Department of Statistics (DANE),

prevalences are estimated, a heat map and a Regression are performed Simple and multiple Poisson with robust variance, adjusted for sex, age, life cycle and region.

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Discussion: The data obtained in this study differ from those published by the control entities.

Conclusions: Quantitative and mixed research should be promoted, as well as a recoding of the diagnoses identified as orphan disease.

Keywords: orphan diseases, coding, prevalence.

1. A worldwide recognition

Orphan diseases are a global problem, therefore, many efforts have focused on their identification, diagnosis and treatment; the Asian continent was the first since Japan in 1972, with the creation of a program for research in rare diseases and patient care [1], on the other hand, in China the patient organization (China-Dolls Care and Support Association) started a voluntary registry in 2010 with more than 30 registered diseases and more than 3,000 patient cases, which today has 32 projects involving rare diseases and one with 1,000 Mendelian Disorders [2].

In Europe, Spain took the initiative in 1996 with the creation of the Research Center on Toxic Oil Syndrome at the Carlos III Health Institute, which in 2000 became the Research Center for Toxic Oil Syndrome and diseases by Ministerial order. rare [3]. France, for its part, was the first country in the European Union to host policies on rare diseases in 2004, Portugal followed in 2008, Germany in 2010 and the United Kingdom in 2012 [4].

The United States in the American continent in 1993, creates the office for rare diseases and research, later in November 2002 to establish the amendment on rare diseases (Public Law 107-280) [5]. Argentina in 2001, creates the liaison group, Research and Support-Rare Diseases at the regional level; In Brazil, the first Ibero-American Congress on Rare Diseases was held in 2013, and in October of this year a working group was formed to create a national system for patients with Rare Diseases [4].

In Colombia, with the issuance of Law 1392 of 2010, orphan diseases are recognized as of special interest [6]; With this, the regulations begin to regulate the issue with Law 1438 of 2011, Decree 1954 of 2012, agreement 537, resolutions 430 and 3681 of 2013, resolution 1147 of 2014, circular 049, resolution 2048 of 2015, circular 011, circular 022, decree 780 of 2016, circular 0008 and 0009 of 2017, circular 0012, resolution 651 and resolution 5265 of 2018 by which the list of orphan diseases is updated and other provisions are issued [7].

1.1 How did Colombia start?

Law 1392 of 2010 is a set of 16 articles that deal with the proposed action for financing, actors and actions, scientific knowledge, inspection, surveillance and control for orphan diseases in Colombia [6]. The importance of a first exercise to capture and systematize national information on patients with these diagnoses not only resides in the technical, public policy and scientific dimensions, but it is also an exercise that has helped to build trust between actors, and ¬gitimacy among the health sector [8]. For this reason, and according to decree 1954 of 2012 [9] and subsequent to the list contained in resolution 430 of 2013 [10], the national census of orphan diseases in Colombia 2013 led by the High Cost Account, which It had the report of all health entities nationwide.

In short, a great first step where 13,173 patients with orphan diseases were found by 2013 [4], which suggests the need to create the District Technical Board for Orphan Diseases as a result of resolution 1147 of 2014 and in compliance with the Article 7 of Agreement 537 of 2013 [11]; Later in 2015 and led by the Directorate for the Regulation of Benefits, Costs and Rates of Health Insurance, the nomination, selection and prioritization of Health Technologies (TS) were made, which were finally studied by the Institute for Technological Evaluation in Health-IETS, Likewise, in its last part, the results of these evaluations are condensed and the technologies proposed for inclusion in the Benefits Plan are listed [12].

Hence, in 2016 circular 011 was issued, aimed at ensuring that patients receive the specialized care they require, so it is necessary to guarantee adequate and sufficient human talent, allowing there to be timely, comprehensive and quality access to technologies and drugs, and always guaranteeing the continuity of their treatments [8].

1.2 About encoding

According to article 140 of Law 1438 of 2011 that modifies the definition contained in article 2 of Law 1392 of 2010 [14]:

> “Orphan diseases are those chronically debilitating, serious, life-threatening and with a prevalence of less than 1 in every 5,000 people, including rare, ultra-orphan and neglected diseases. Neglected diseases are typical of developing countries and ordinarily affect the poorest population and do not have effective or adequate treatments accessible to the affected population ”.

Each time the list of orphan diseases is updated, it has an interdisciplinary group of experts who evaluate each case before including or ruling it out; For the last update, in May 2017, it began with the reception of applications, which were

published in June, they were evaluated in July, in September the results and the draft resolution were published for public consultation [15], after a long process for its acceptance, on November 27, 2018 resolution 5265 was born with a list of 2190; 2088 grouped and classified into 579 ICD-10 codes and 102 without classification code [16].

An ICD-10 code can have between 1 and 284 orphan diseases, this classification was made with reference to the type of disease, anatomical location and type of affectation, due to its low prevalence orphan diseases are not registered in this world classification, however, the In order to specify diagnoses, treatment and report, the evaluating group carried out their grouping. In such a way that most of the codes do not coincide in the name of the disease and only in the report to SIVIGILA [16], it can be specified and supported with diagnostic evaluations.

Thus, we found a classification drawback that in real life can be unmanageable, for example, the ICD-10 code Q788 - Other specified osteochondrodysplasias, to which 21 orphan diseases are attributed or the code G318-Other specified degenerative diseases of the system nervous system with 16 types of classified diseases [7]. In rural areas where a medical resident is the only health contact and the most innovative technology is a stethoscope, in short, the professional could not be blamed for a bad diagnosis; While it is true that the joint efforts of the health sector have reduced multiple access barriers, it is also true that there is still too much to make visible orphan diseases in Colombia.

2. objective

Carry out a prevalence analysis, using databases that are freely accessible to the general public, comparing them with the reports made by the entities in charge of managing the data for the capture, diagnosis and management of orphan diseases in Colombia.

3. Materials and methods

A cross-sectional study was carried out, using as a source the RIPS 2015 - 2018 databases generated by the SISPRO Cubes [17], 24 bases were obtained with a total of 368,570,968 people attended per year, sex, five-year age, type affiliation and department, corresponding to 11,733 diagnoses in grouped presentation; undefined information for all variables is discarded.

Given that, due to the type of grouped classification, there may be an under-registration at the time of the systematization of the cases, due to the ignorance of the health personnel, deficit of diagnostic technologies and erroneous classification of the patients; This study takes only 319 diagnoses of the 578 contained in resolution 5265 of 2018, which correspond to a single type of orphan disease, the 102 diagnoses without coding are also eliminated from the cross, as well as, the people attended by the A81, D57 .-, D685 and K850 not found in the ICD-10 at the time of verification.

Once the initial base is crossed, the result is a base with 3,014,555 people treated for a diagnosis of orphan disease during the years 2015 - 2018 in grouped presentation. The region and life cycle variables are added to this base, the latter corresponds to early childhood (0-4 years), Childhood (5-9 years), adolescence (10-19 years), youth (20-29 years), adulthood (30-59 years) and old age (≥60 years), according to the life cycle classification of the Ministry of Health and Social Security [18]; The foregoing, insofar as an orphan disease is of a biological type, therefore, the changes inherent in the individual's life cycle can affect its appearance.

Finally there are 4 ungrouped bases: 2015 (639474), 2016 (653247), 2017 (783110), 2018 (938724); classified by sex, life cycle, region and type of affiliation: subsidized - contributory. The population projection of the DANE 2005 [19] and the historical coverage of the SGSSS [20], were taken as total populations to estimate the prevalences.

For the mortality rate, the microdata of the vital statistics 2015 - 2018 generated by DANE [19] are taken; Two bases are obtained, one of fetal deaths with 182939 and one of non-fetals with 907106 ungrouped records; Once the variables of interest are extracted, they are crossed with the 319 codes in the 12 variables of causes of death. For the extraction of data object of analysis, only the variables with the greatest number of coincidences (basic cause and direct cause) were taken; leaving a base of 21882 ungrouped records.

The databases were downloaded and organized in the Excel computer program [20] and subsequently analyzed in Stata MP 13 [21] (Poisson regression), Epidat_4.1 [22] (mortality rates) and Epi Map 7.2® [23] (heat map).

4. Results

Information was collected from 2015 to 2018, from which a final population of 3,014,555 people cared for one of the 319 diagnoses of orphan diseases under study was obtained. Table I shows the 10 most frequent diseases versus the 10 least frequent.

In the heat map (Fig. I), a higher prevalence is observed in females (58.9%), as well as in the department of Bogotá (28%), followed by Antioquia (19.3%) and Valle del Cauca (8.9%). The prevalence by region was lower in Amazonía (n-21685 = 0.7%) followed by Orinoquía (n-1 41704 = 4.7%), Caribe (n- 391384 = 12.9%), Pacífico (n- 418748 = 13.8%) and Andina (n- 2141 034 = 71%).

Table II describes the proportion of gross and period prevalences per 1000 inhabitants per year and variables analyzed, the year with the most cases was 2018 (n- 938724 = 31.1%), 70 women per 1000 had an orphan disease between 2015 and 2018, 24 out of every 1000 inhabitants of the Andean region had an orphan disease in 2018, the highest prevalence was in the Old Age age group, 144 out of every 1000 inhabitants over 60 years old, had an Orphan disease in the period of interest, the largest number of people treated for orphan diseases during

the period were mostly affiliated to the contributory scheme (n = 2182147 = 72.3%).

Next, in table III the summary of data produced by the simple Poisson regression and multiple Poisson regression with robust variance is presented, the reference values were male, early childhood and Amazonía given its lowest.

Being a woman is 0.94 times associated with having an orphan disease, belonging to the life cycle of old age increases the probability of having an orphan disease by 2.03 times, belonging to the Andean region adjusted for sex and age is 4.19 times associated with having an orphan disease. In 2015 and 2016, being between 10 and 19 years old is not statistically significant in the probability of having an orphan disease. Belonging to the Andean and Caribe regions in 2018 is not statistically associated with having an orphan disease.

Table IV shows the data on the crude and adjusted mortality rates by region, which were standardized with the population of the year 2017. The highest rate is in the Andean region with 0.12% and the lowest in the In the Amazonía region with 0.05%, the latter in line with the lowest prevalence of cases in the region, no significant differences are observed between the crude and adjusted rates.

5. Discussion

To make a problem visible, it is necessary to create simple, complete and freely accessible information systems, contributing to the investigation of new technologies and strategies, which, in addition to recognizing the difficulties, lead to their improvement. Continuing with the objective of this study; Colombia lacks research on orphan diseases, which have emerged tepidly as a result of legal considerations that penalize their non-intervention, but which have not transcended from the report to the transformation.

To this end, an analysis of information available at the national level is carried out, which is the object of statistical research in most health fields and is compared with

the published data of entities in charge of the surveillance and control of this type of diagnosis, such as it is, the high-cost account [25] and the National Institute of Health [26].

In the balance of surveillance in public health 2016-2018 [27], the prevalence ratio in 2016 was 1.4 per 100,000 people and in 2017 it was 6.3 per 100,000 people. In this study in 2016 the proportion was 13 per 1000 people in 2016 and 16 per 1000 people in 2017. It should be clarified that this study was carried out with information from the diagnoses of people treated, however and these diseases being little common it is undeniable that underreporting is occurring, the question is what motivates this.

On the other hand, we found that the highest prevalence was concentrated in the female sex (58.9%), which is similar in the national census where it was 53.96% [4], however in the balance of surveillance the highest proportion was in men (61.7%) [27] as well as in the report of event 342 of 2017 [28]: the proportion of prevalence by sex was higher in males, being even slightly higher than the national prevalence, however, and Also referred to in said report, the heterogeneity of the orphan diseases reported does not allow us to explain this behavior.

The old age life cycle was present in greater proportions during all the years of study compared to the national census, where the median age was 28 years with an inter-quartile range of 39 years. As for the XIII period of 2018, according to the Rare-orphan disease surveillance event report, being older than 65 years had a higher prevalence, the information is also equivalent to the low prevalence in early childhood (2.5%) [29]. At this point, the need arises to study each diagnosis more in depth, in order to determine if the high prevalence is due to its occurrence only in advanced ages or to the delay and access barriers for the confirmation of the diagnosis, in the same way in the first childhood.

Faced with georeferencing, we found that the department of Bogotá, in this as in the comparison reports already mentioned, had the highest prevalence. Here it is necessary to recall a statement in the introduction of this article regarding the situation of a rural doctor in a place without technology and what makes his work difficult, as well as the statistically significant results in the Poisson regression in the section on the regions, to rethink that the high prevalence is due more to access to diagnostic technologies, than to belonging to a certain region. Regarding regions, the data is maintained with the others, with the Andean region having the highest prevalence in all the reports and the Amazonía region the lowest.

Another interesting issue is the marked distance between the prevalence of the contributory regime (72%) and the subsidized one (28%); One of the causes for a disease to be an orphan is the difficulty from all areas for its diagnosis, therefore, if we see it from a social and economic perspective where the stratum determines a type of access to health, sources of transport, food, among others, this data must be preceded by social level.

6. Conclusions

In the bibliographic search of this article, it is evident that most of the studies are qualitative, however, the balance must be balanced in the face of this problem and promoting quantitative and mixed research, which provides an accurate systematization that leads to timely diagnoses and without access barriers and therefore to quality care.

Colombia still does not have an information system that allows freely and without confusion to identify the prevalence of orphan diseases, it is necessary to recode diagnoses with its own code that is almost easy to identify at the national level.

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Bogota D.C., January 15, 2021

Sirs

Editors Health care management science magazine Regards,

This is to send you the manuscript The National Recoding of Orphan Diseases: A Proposal Directed to Health Care, for its evaluation and publication as an original article to be considered.

It is evident that this article has not been published or sent for review in another journal and that all the authors meet the sufficient criteria to appear as authors.

We are attentive to your reply.

We thank you in advance for your attention,

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