British Journal of Healthcare and Medical Research - Vol. 11, No. 1
Publication Date: February 25, 2024
DOI:10.14738/bjhmr.111.16353.
Pérez, S. P., Cameselle-Cortizo, L., Cruz, T. C., Rodríguez-Fernández, V., & Cameselle-Teijeiro, J. F. (2024). It is Necessary to Increase the Training and Motivation of Primary Care Health Professionals in the Face of Rare Diseases in Spain. British Journal of Healthcare and Medical Research, Vol - 11(1). 171-179.

It is Necessary to Increase the Training and Motivation of Primary Care Health Professionals in the Face of Rare Diseases in Spain

Susana Portela Pérez
Clinical Oncology Research Center ADICAM. Cangas (Spain) and
IVI Vigo. Assisted Reproduction and Fertility Clinic. Vigo (Spain)

Lucía Cameselle-Cortizo
Clinical Oncology Research Center ADICAM. Cangas (Spain) and
Geriatric Service. Vigo University Hospital Complex. Vigo (Spain)

Teresa Calheiros Cruz
Clinical Oncology Research Center ADICAM. Cangas (Spain)

Vanesa Rodríguez-Fernández
Clinical Oncology Research Center ADICAM. Cangas (Spain)
and Obstetrics and Gynecology Service. Breast Pathology
Unit. Vigo University Hospital Complex. Vigo (Spain)

Jorge F Cameselle-Teijeiro
Clinical Oncology Research Center ADICAM. Cangas (Spain)

ABSTRACT

Background: Rare diseases (RDs) are defined as low prevalence diseases with great heterogeneity. Globally, they constitute an important public health problem. Most of them are incurable, chronic and have a great family impact. The objective of this study was to investigate the knowledge about RDs among primary care health professionals (137 doctors and 113 nurses) in our health area (Vigo, Spain). Methods: A total of 250 primary care health professionals, randomly chosen, completed an anonymous survey to evaluate their level of knowledge about aspects related to RDs. The survey contained a questionnaire (seven questions) related to basic aspects of rare diseases. Results: Primary care health professionals showed very poor knowledge about the impact of RDs on public health. There were no statistically significant differences when comparing the responses of doctors versus nurses in any of the responses obtained ($p > 0.05$). Conclusions: Among the main challenges facing RDs is shortening the diagnostic delay and providing comprehensive care. Primary care health professionals should play a key role, since they are the gateway to the health system. Unfortunately, the results of our survey reveal very poor knowledge about basic aspects of RDs. It is necessary to increase training and motivation if we want to improve the health care provided from primary care to patients with RDs.

Keywords: Rare Diseases, Medical Training, Primary Health Care, Clinical Genetics.

INTRODUCTION

RDs are defined as minority or low prevalence diseases with great heterogeneity. Although individually they are rare, as a whole (they are a considerable group of pathologies, between 5,000 to 8,000 depending on the type of classification) they affect a large group of the population: 3,000,000 people in Spain and 29,000,000-30,000,000 people in 48 European countries. Simple statistical data justify us considering RDs as an important public health problem, but this problem is aggravated if we consider that a large majority are incurable, that is, "they are for life" and transcend the personal sphere, having a "great family impact". The symptoms (symptoms and/or signs) of the vast majority of RDs occur during childhood and around 70-80% of these are hereditary. 75% of RDs affect children. 70% of RDs have their onset during childhood.

Most RDs are genetic diseases; others are rare cancers, autoimmune diseases, congenital malformations or toxic and infectious diseases, among other categories. Accepting the great differences in terms of etiology, pathogenesis, pathophysiology, diagnosis, prognosis, treatment and prevention, they share a series of characteristics that make them a differentiated group of clinical medicine: they are low prevalence diseases, with a mostly genetic origin and little scientific knowledge, they associate diagnostic delay, a feeling of helplessness and loneliness, chronicity and also dependence on the health system.

The geographical dispersion of affected people and the difficulties in obtaining information related to genetic data are a real problem. The main challenges are to shorten the diagnostic delay, generate tools for the training of health professionals, make RDs visible, promote specialized centers and effective therapeutic interventions. The high cost of some drugs, the high associated morbidity and mortality, the chronic support needs (electric wheelchairs, stimulation and rehabilitation sessions, etc.) and the lack of coverage of some of these resources by public health systems burden the affected families.

Statement of the Problem

We have to make an extra effort to improve the prevention of RDs, social health care and treatments. It is very important to detect warning signs early, direct and accelerate consultations with hospital care, and coordinate follow-up. Primary health care can bring together comprehensive action, thus improving the quality of life of the patient and their family environment. Advances in the medical approach to rare diseases run parallel to advances in clinical and molecular genetics and even artificial intelligence. Seven out of 10 people with RDs force a family member to reduce or suspend their professional activity to help care for them.

In Spain, each primary care physician has an approximate quota of 1,400 people. Primary care physicians are the gateway to the National Health System for any type of disease and can play a key role in the diagnosis, management and treatment of patients with RDs. We plan to investigate the level of knowledge of primary care health professionals (doctors and nurses) in our health area (Vigo, Spain) in relation to RDs.

Research/Survey Questions

1. In Europe, what is the correct definition of a rare disease?

2. Do you know the incidence of rare diseases in our autonomous community (Galicia, Spain)?
3. How many different types of rare diseases are there?
4. What is the approximate number of people affected with a rare disease that each primary care physician has in their quota (average of 1,400 users per doctor) in our health area?
5. What do you think is the approximate average diagnostic delay for rare diseases globally?
6. What percentage of rare diseases are hereditary?
7. What approximate percentage of Europeans are healthy carriers of cystic fibrosis?

METHODS

Research Design

The study adopted a cross-sectional research design to evaluate the knowledge of primary care health professionals (doctors and nurses) about RDs.

Target Population and Sampling Technique

A total of 250 primary care health professionals from the health area of Vigo (Spain) were randomly chosen at random (Table 1) to complete an anonymous survey with the aim of evaluating the level of current knowledge about some aspects related to RDs. The survey contained a very basic questionnaire (seven questions) that professionals had to complete in a short period of time in the presence of the interviewer, which was intended to investigate, through simple questions, the level of knowledge about RDs in primary health care. Of the total of 250 health professionals: 54.8% were doctors and 45.2% were nurses. The current feminization of our profession is confirmed, since more than two thirds of those interviewed (77.2%) were women. This percentage was majority among nursing professionals (92.9% women vs. 7.1% men).

Professional category	Total	Men	Women
NURSES	n = 113 (45.2%)	n = 8 (7.1%)	n = 105 (92.9%)
DOCTORS	n = 137 (54.8%)	n = 49 (35.8%)	n = 88 (64.2%)
Total	n = 250 (100%)	n = 57 (22.8%)	n = 193 (77.2%)

- Inclusion Criteria: Doctor or Nurse, regardless of gender, who works in primary health care and has more than five years of active experience in our healthcare area.
- Exclusion Criteria: Less than five years of experience in primary health care.

The Health Area of Vigo and surrounding areas (Figure 1) encompasses an approximate population of half a million people. It includes a total of 17 Health Centers and an Out-of-Hospital Emergency Service in the city of Vigo itself (300,000 inhabitants) and 12 Health Centers with some Out-of-Hospital Emergency Services located in 12 peripheral towns in the same region: A Guarda (10,000 inhabitants), A Cañiza (5,000 inhabitants), Cangas (27,000 inhabitants), Moaña (19,000 inhabitants), Porriño (20,000 inhabitants), Ponteareas (23,000 inhabitants), Redondela (29,000 inhabitants), Tui (17,000 inhabitants), Tomiño (14,000 inhabitants) , Baiona (12,000 inhabitants), Gondomar (15,000 inhabitants) and Nigrán (18,000 inhabitants).

URL: http://dx.doi.org/10.14738/bjhmr.111.16353.

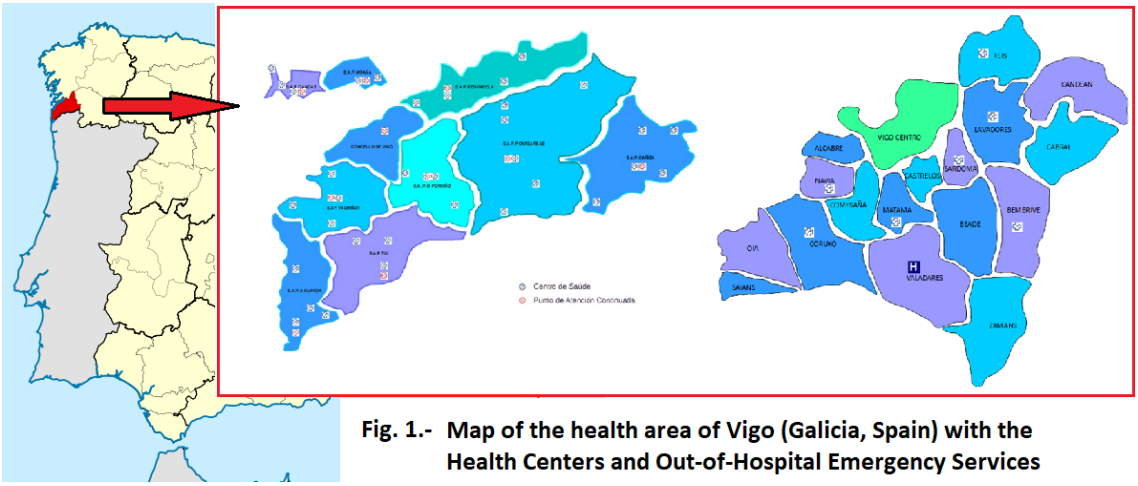


Fig. 1.- Map of the health area of Vigo (Galicia, Spain) with the Health Centers and Out-of-Hospital Emergency Services

Data Analysis

Data were entered into a database and SPSS for Windows (version 26) was used for data analysis. The data were expressed as frequency and percentage for each variable. The chi-square test was then used to examine the association between variables. $P < 0.05$ was considered statistically significant.

Ethical Considerations

The study adhered to the ethical principles of the Research Ethics Committee. The principal investigator obtained ethical approval from the Institutional Review Board after providing a full explanation of the purpose and nature of the study. Written informed consent was obtained from the study samples after providing them with details about the nature of the study, benefits, and risks. They were informed that participation in the study is voluntary and they have the right to withdraw without liability. Additionally, they were assured that their data was encrypted and that their personal information was kept confidential. There was no link between your personal information and the published data.

RESULTS

Demographic Characteristics of the Study Participants

A total of 250 health professionals were interviewed: 137 (54.8%) were doctors and 113 (45.2%) were nurses. 77.2% were women (Table 1). No one refused to participate in the survey. Table 2 shows the percentage of correct answers in each of the questions.

QUESTIONS	CORRECT ANSWERS
1. In Europe, what is the correct definition of a rare disease?	**29,6 %** (n = 74 de 250)
2. Do you know the incidence of rare diseases in Galicia?	**13,6 %** (n = 34 de 250)
3. How many different types of rare diseases are there?	**30,0 %** (n = 75 de 250)
4. What is the approximate number of people affected with a rare disease that each primary care physician has in their quota (average of 1,400 users per doctor) in our health area?	**16,0 %** (n = 40 de 250)
5. What do you think is the approximate average diagnostic delay for rare diseases globally?	**75,2 %** (n = 188 de 250)
6. What percentage of rare diseases are hereditary?	**31,6 %** (n = 79 de 250)
7. What percentage of Europeans are healthy carriers of cystic fibrosis?	**40,0 %** (n = 100 de 250)

DISCUSSION

Overview of Main Findings

The result of the current study (Table 2) shows that globally, primary care health professionals in our health area have very poor knowledge about the impact of RDs on public health. No statistically significant differences were recorded when comparing the responses of doctors versus nursing staff in any of the responses obtained ($p > 0.05$).

In Europe, What is the Correct Definition of a RD?

The Community Action Program on Rare Diseases (1999-2003) adopted the current definition of "rare diseases" as those with a prevalence of no more than 5 per 10,000 in the European Union. The same definition is established in Regulation (EC) No 141/2000 and is therefore also used by the European Commission for the designation of orphan medicinal products. RD is defined by the European Union as a disease that affects one patient per 20,000 inhabitants (1). Additionally, RDs have a clinical criterion that completes their definition as serious, chronic diseases that entail some type of disability or high mortality.

RDs are defined, fundamentally, by their low prevalence in society, not by the organs or parts of the body that they affect. We were very struck by the lack of knowledge of health professionals regarding a question, theoretically so simple, that in itself defines the group of diseases of this type. Only one in three primary care health professionals (30%) knew how to correctly define the meaning of a RD. Some based the definition of a RD, incorrectly, on clinical diagnostic criteria. Others in erroneous prevalence figures.

However, our results coincide with the findings published in 2012 by the Rare Diseases Working Group of Spanish Society of Primary Care Physicians (2), who, in a survey of 260 primary care physicians in Spain on the perception of RDs, already warned that only 20.4% of the doctors at the Health Centers had specific training related to RDs.

The term “rare” refers to its low prevalence in the population compared to the most common pathologies. The adjective comes from an Anglicism “rare disease” that should be interpreted in its meaning of “infrequent”, but not as something strange or exotic. The wide diversity of symptoms and signs varies not only from one rare disease to another but also from one patient to another suffering from the same disease. Therefore, perhaps it would be more accurate to call them minority diseases, low prevalence, low frequency or also refer to them as orphan diseases. They have been neglected for too long and despised by clinicians, medical researchers, the pharmaceutical industry and also by society globally. However, this definition (1: 2,000 inhabitants) valid for Europe is not universal. The legal definition varies from one geographic area to another depending on the prevalence defined in each area: Australia (1: 10,000 inhabitants), Japan (1: 2,500 inhabitants), China (1: 1,315 inhabitants) and the United States (1: 1,250 inhabitants). We must also keep in mind that a disease may be rare in one region, but common in another. For example, the term ultra-rare disease is reserved for when the prevalence of the disease is less than 1: 50,000 inhabitants.

Do You Know the Incidence of RDs in Our Autonomous Community (Galicia, Spain)?

Only one in ten primary care health professionals (30%) correctly estimated the incidence of RDs in the Autonomous Community of Galicia (Spain). The vast majority of health professionals underestimated the incidence with much lower figures.

URL: http://dx.doi.org/10.14738/bjhmr.111.16353.

The truth is that, although the number of individuals affected by each of the rare diseases is very small, overall, the number of RDs is very high (3), which means that there are many more rare diseases than common. RDs affect, as a whole, 6% of the European population (about 3 million in Spain, about 33 million in Europe), 30 million North Americans and over 500 million in the world. So, one in 17 people will be affected by a RD at some point in their life. Other authors point to a slightly lower percentage, 4% of the population during their lifetime, with estimates that range between 3.5% and 5.9% (3).

In Galicia it is estimated that there are approximately 200,000 people affected by a RD (4).

How Many Different Types of RDs are There?

Only one in three primary care health professionals (30%) responded that there are between 5,000-8,000 different types of RDs, depending on the definitions and classifications used: Online Mendelian Inheritance in Man (OMIM) (5). The WHO collects around 5,500 (6) RDs, the National Institute of Health (NIH) of the United States around 7,000 (7), the European Commission reports between 6,000 and 8,000 (8), and EURORDIS estimates them at 6,000 (9). The majority (70%) of responses underestimated the actual number by well below the accepted estimate. This fact represents a serious problem, since not being aware of its real impact and there being such a high number of different diseases (more than 5,000) increases the lack of interest in them.

There are many difficulties in knowing with certainty the prevalence or specific incidence of any of the Rare Diseases since they are not reported, not diagnosed or are incorrectly diagnosed. However, based on the population as a whole affected by all these pathologies, we know that in Spain there are more than three million affected. According to data from the Directorate General for Health and Consumer Protection of the European Commission, these diseases affect up to six percent of the total population of the European Union, at some point in their lives (10).

What is the Approximate Number of People Affected with a RD that Each Primary Care Physician has in their Quota (average of 1,400 users per doctor) in Our Health Area?

Posada et al. (11) estimate that the number of users with a RD within a standard quota of 1,400 users ranges between 15 and 20, depending on the prevalence. Just as we know the needs of our patients with common chronic diseases, which occupy almost half of our daily work, the Spanish Society of Family and Community Medicine recommends that each doctor update their knowledge of the specific RDs of their patients, knowing that the best source of information is usually themselves, since the patient with a RD is the paradigm of the informed chronic patient.

Although it is true that it is estimated that 80% of RDs are of genetic origin, 3 out of 4 can be diagnosed clinically, without impairing the usefulness of genetic counseling. Therefore, nothing prevents the primary care professional from suspecting the presence of any of these diseases based on a series of signs or symptoms that do not quite fit with the most prevalent conditions (12).

The answer accepted as correct in our survey was 15 to 20 people with RDs. The correct answer was only provided by 16% of health professionals. We are concerned by the evidence that 84% of primary healthcare professionals underestimated the number of users with a RD that they

could have in their quota. Eight out of 10 responded that they did not have any users with a RD in their quota or if they did, this figure was less than 5 among the 1,500-2,000 users. It is essential to modify this "little awareness" about the reality of RDs and this gives meaning to our research.

Training on RDs must be specific in its content and differentiated for hospital and health center professionals. Knowledge of the classic pathognomonic signs is necessary (13). Conceptual maps are useful for diagnosing RDs in primary care (14).

What Do You Think is the Approximate Average Diagnostic Delay for RDs Globally?

The average diagnostic delay for RDs is 5 years. 70% of people with RDs wait more than 1 year for a confirmed diagnosis after seeking medical care (9). Three out of four (75%) primary care health professionals answered this question correctly. The lack of specific health policies for rare diseases and the shortage of specialized knowledge generates delays in diagnosis and difficulties in accessing care. This leads to an accumulation of physical, psychological and intellectual deficiencies, inadequate or even harmful treatments and loss of confidence in the healthcare system, even though some RDs are compatible with a normal life if diagnosed early and addressed correctly. Misdiagnosis and lack of diagnosis are the main obstacles to improving the quality of life of thousands of patients with RDs.

What Percentage of Rare Diseases Are Hereditary?

Around 70-80% of RDs have a genetic transmission (Mendelian inheritance). The correct answer was only provided by one in three (31.6%) of the professionals surveyed.

24% of RDs have an autosomal dominant inheritance, 35% are recessive, 7% are due to chromosomal anomalies, 5% have a dominant or recessive origin, 5% depend on a recessive inheritance linked to the X chromosome and 1% a dominant inheritance linked to the X chromosome. A smaller group have mitochondrial transmission, are multigenic/multifactorial or with a multiple inheritance pattern (3).

What Approximate Percentage of Europeans are Healthy Carriers of Cystic Fibrosis?

Approximately, between 2-3% of people are born with some genetic alteration (15). In the specific case of cystic fibrosis, since it is a disease with autosomal recessive inheritance, the risk of being a healthy carrier is based on your personal and family history of cystic fibrosis: 100% risk for the parents of a sick child. In the healthy population without a family history, this risk varies by ethnic group (1 in 24 Ashkenazi Jews, 1 in 46 Hispanic Americans and African Americans, and 1 in 94 Asians). In northern Europe this risk is 1 in 25 healthy people; while in Galicia (Spain) the risk of being a healthy carrier is lower but considerably high (1 in every 35 people). 40% of the health professionals surveyed answered this question correctly. The recommendations at that time are that carrier screening (genetic compatibility testing) be offered to population groups of Ashkenazi Jewish descent and also to the European population, especially in northern Europe because they have the highest carrier frequencies (16-20).

CONCLUSION

Clinical genetics and molecular biology are already a reality in Medicine. However, primary health care is taking a long time to assimilate those genetics is already the medicine of the present and, above all, the medicine of the future (21). A recent review (22) that included 80

URL: http://dx.doi.org/10.14738/bjhmr.111.16353.

publications showed that primary care is essential to approach patients with RDs, mainly due to the ease with which it can offer longitudinal, multidisciplinary and coordinated care. This same article agrees that current medical training is insufficient.

Among the main challenges facing RDs is shortening the diagnostic delay and providing them with comprehensive care. Primary care health professionals should play a key role, since they are the gateway to the health system. Unfortunately, the results of our survey reveal very poor knowledge of basic aspects. It is necessary to increase training and motivation if we want to improve the health care provided to patients with RDs from primary care.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Funding

All authors have no source of funding.

References

1. Posada M, Alonso-Ferreira V, Sánchez EB. Enfermedades raras. 1a ed. Los Libros de la Catarata; 2016)

2. Avellaneda Fernández A, Pérez Martín A, Pombo Allés G, Gutiérrez Delgado E, Izquierdo Martínez M. Grupo de Trabajo de Enfermedades Raras de Semergen. Percepción de las enfermedades raras por el médico de atención primaria [Perception of rare diseases by the primary care physicians]. Semergen. 2012; 38(7):421-431.

3. Nguengang Wakap, S., Lambert, DM, Olry, A. et al. Estimación de la prevalencia puntual acumulada de enfermedades raras: análisis de la base de datos Orphanet. Eur J Hum Genet 2020; 28: 165-173.

4. FEGEREC. Federación Gallega de Enfermedades Raras e Crónicas. https://fegerec.es/enfermedades-raras-que-son-es.html.

5. Online Mendelian Inheritance in Man: htpps://www.omim.orge/.

6. https://who.int/standards/classifications/frequently-asked-questions/rare-diseases.

7. https://rarediseases.info.nih.gov/about.

8. https://ec.europa.eu/info/research-and-innovation/research-area/health-research-and-innovation/rare-diseases_en.

9. https://eurordis.org/information-support/what-is-a-rare-disease/

10. Posada M, Izquierdo M, Ferrari, MJ, Avellaneda A, Andrés P, et al. Plan de Acción de la UE y del Estado Español sobre enfermedades de baja prevalencia. . Boletín del Real Patronato sobre Discapacidad. 2002; 53:25-29.

11. Posada de la Paz M, M. GRF. Enfermedades raras: concepto, epidemiología, situación actual y perspectivas futuras. . Aten Primaria 2010; 42:169-172.

12. García-Ribes M. El diagnóstico de las enfermedades raras desde la consulta de Atención Primaria: desmontando el mito (The diagnosis of rare diseases in the primary care clínic: Dismantling the myth). Aten Primaria 2013; 45(7):338-340).

13. Smith CS, Paauw DS. When you hear hoof beats: four principles for separating zebras from horses. J Am Board Fam Pract 2000; 13:424-429.

14. Ortega Calvo M, Gómez-Chaparro Moreno JL, González-Meneses López A, Guillén Enríquez J, Varo Baena A, Fernández de la Mota E. Mapas conceptuales para el diagnóstico de las Enfermedades Raras en Atención Primaria. Aten Primaria 2012; 44(1):43-50).

15. Simpson JL, Rechitsky S, Kuliev A. Fertil Steril 2019; 112:622-630.

16. Pastor-Vivero, M. (2021). Spanish Cystic Fibrosis Registry: Report 2018. *Spanish Cystic Fibrosis Society Registry Group*. https://fibrosisquistica.org/wp-content/uploads/2021/04/Report2018-definitivo-4.pdf

17. Richards CS, Bradley LA, Amos J, et al. Standards and guidelines for CFTR mutation testing. Genet Med. 2002:4:379-391.

18. Watson, Michael S., et al. Cystic fibrosis population carrier screening: 2004 revision of American College of Medical Genetics mutation panel. Genetics in medicine 2004; 6:387-391.

19. Updated recommendations for *CFTR* carrier screening: A position statement of the American College of Medical Genetics and Genomics (ACMG) Genetics in Medicine 2023; 25: 100867

20. J.L. Deignan, C. Astbury, G.R. Cutting, *et al.* CFTR variant testing: a technical standard of the American College of Medical Genetics and Genomics (ACMG). Genet Med, 2020; 22(8): 1288-1295, 10.1038/s41436-020-0822-5

21. Emery J, Hayflick S. The challenge of integrating genetic medicine into primary care. BMJ. 2001; 322:1027-1030.

22. Ferreira RL, do Nascimento IJB, de Almeida VIA, de Oliveira VRL, Marangne LG, Dos Santos Gameleira F, Dutra TRC, de Oliveira Santos D, Dias Afonso MP, Dos Santos PEA, de Oliveira HN, Vilhena Dias FM. The utilisation of primary health care system concepts positively impacts the assistance of patients with rare diseases despite limited knowledge and experience by health care professionals: A qualitative synopsis of the evidence including approximately 78 000 individuals. J Glob Health. 2023 Aug 4; 13:04030. doi: 10.7189/jogh.13.04030. PMID: 37539555; PMCID: PMC10401310.