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PERSPECTIVES ON THE IMPACT OF ROMANIAN PATIENT ORGANIZATIONS IN RARE ENDOCRINE DISEASES

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Abstract: *Introduction.* Rare diseases (RDs) are pathologies that affect a small number of people compared to the general population. In the literature we discover a general approach on rare diseases (RDs), most studies observing a single pathology or the whole spectrum. The current study follows a specialty-based approach of endocrine RDs. This study evaluates the ways in which patients and doctors relate to patient organizations (POs), including education and involvement in research activities.

Methods. A questionnaire was applied between May 20th and June 30th 2020 to 66 endocrinologists and to 32 patients with a rare endocrine disease.

Results. RDs cause significant burdens for patients and their families, especially from a mental health perspective. The most significant activities of POs for patients are provision of medical education, legal counsel, advocacy and policy-making, whilst doctors consider mental health support as the main role. While a majority of patients collaborate with organizations, only 11% of Romanian endocrinologists do so, the main cause being the insufficient knowledge about these structures. Patient involvement is considered by both groups to be needed in RDs research, but 69% of patients were never part of a research study due to lack of information.

Conclusions. POs play a key role in the management of RDs and more physicians should be involved in their activities. Studies on larger groups should be conducted prior to coherent policy-making in this field.

Keywords: rare diseases, orphan diseases, patient, healthcare professional, research, case management, endocrine system diseases, patient organizations, integrative medicine, medical education.

INTRODUCTION

Rare diseases (RDs) are pathologies that affect a small number of people compared to the general population. In Europe, a disease is considered rare when it affects 1 person in 2000. The term can also refer to the region, with the frequency of certain diseases varying from region to region. There are also many common diseases whose pathological variants may be rare. These diseases raise problems specific to their rarity. Rare diseases affect not only the person diagnosed, but also their families, healthcare providers and society in general. Many of them are called orphan diseases because the people affected by them do not yet receive adequate treatment and integrated management from the health system [1, 2].

In Romania, approximately 1.3 million people suffer from RDs. The greatest impact is on children and families because 75% of these pathologies are present at birth or debut before the age of 2. Other RDs, about 25% of them, have an onset around the age of 40. These pathologies are accompanied by a significant impact on life expectancy, while in over 65% of cases the disease affects the daily routine or limits the patient's autonomy [3, 4].

Studies show that patients suffering from a rare disease, although belonging to a globally recognized vulnerable group, often become invisible in the healthcare system to which they belong, due to the additional needs of these people, which are not properly

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recognized [5]. The ethical issues faced by patients and healthcare professionals are related to the lack of allocation of resources to these patients, in contrast to more common pathologies. The problem of insufficient care is often raised, including provision of specialized social services, mental health support and appropriate rare drugs [6].

Rare endocrine diseases (REDs) are an important, but often neglected medical field. Rare diseases of interest to endocrinologists involve all areas of endocrinology, namely diseases of the pituitary, thyroid, adrenal and gonads, bone and metabolism disorders and syndromes with possible involvement of multiple endocrine glands and neuroendocrine tumors. The estimated incidence of these rare pathologies is approximately 20-50 / 1,000,000 of which over 90% have a genetic cause [7]. There is no complete and detailed taxonomy of REDs in the literature [8].

Patient organizations (POs) have traditionally provided a supporting role for patients, but their activities are constantly evolving. POs aim to improve the quality of life for patients and their families. Their objectives include raising public awareness of the disease, disseminating information about the disease and its treatment, and promoting scientific research [9]. They can also serve as a mediator between patients, physicians, or other institutions in certain circumstances, demonstrating that patients are aware of the condition they are suffering from, in order to gain recognition, defend their rights, and influence decision-making processes [10].

International institutions, especially the European Union, through the European Strategy for Rare Diseases adopted in 2009 [11], provide priority and sustained support to patient organizations, recognizing their key role in educating the population and case management. Healthcare professionals, in the context in which there is insufficient special training about RDs, cannot constantly know all the details about 8000 such diseases [12]. In Romania, at the moment of this study, there are limited courses dedicated to rare diseases for medical students, the degree of coverage of these pathologies for each medical specialty being very often at the discretion of the teacher. However, patient organizations frequently organize workshops, campaigns, courses and events in order to raise awareness of the need for a comprehensive and integrated approach to RDs, including medical, educational, social support, from childhood to adulthood, for the patients and their families. Moreover POs promote on a regular basis the latest updates and articles related to their patients, having also a positive impact on the continuous education of healthcare professionals [13].

The aim of this study is to evaluate if physicians and patients are involved in POs and in research initiatives, while also analyzing how both groups relate to the various ways in which POs support patients suffering from REDs.

MATERIALS AND METHODS

The study was conducted between May 20th and June 30th 2020, on 32 patients from Romania diagnosed with a rare endocrine disease defined as the first group and 66 endocrinologists from multiple hospitals in Romania with experience in managing RDs, defined as the second group. The data was collected using an online questionnaire. All participants consented for the use of their data for the current study. The survey comprised 7 similar questions for each group, in order to evaluate in a comparative way the opinion of the two studied groups. General data about age, gender, location, profession and experience was collected separately.

Patient and physician responses were centralized in an online database provided by Google services. The data was later exported to Microsoft Office Excel, where it was subsequently analyzed using descriptive statistical methods. Respondents from both groups were selected by sending the questionnaire on various social networks or through patient organizations which collaborated in developing the study.

RESULTS

Patients' attitude towards rare diseases

The first group included 32 patients aged between 1 and 65 years old, 87.5% of them living in urban areas. Patients were diagnosed with a rare endocrine disease, the most common of which are: secondary hyperparathyroidism, rare thyroid neoplasms, neuroendocrine tumors with various locations, Addison's disease, Von Hippel Lindau syndrome, insulinoma, autoimmune thyroid disease, Prader Willi syndrome, osteogenesis imperfecta, multiple endocrine neoplasia type 1. For 25% of the patients a parent or relative was required to fill the survey on behalf of the patient. Of the patients studied, 56% are full-time employees, representing the majority of subjects involved in the study, the other being unemployed (18.8%), retired because of illness (12.5%) or age (6.3%), or studying (6.3%).

Regarding the degree to which the rare endocrine disease affects the daily life of patients, we observe a predominantly small or insignificant impairment in the case of the activities included in the study. The exception is the significant affection of morale and mood (68.75% of the studied patients reported a moderate to very significant mental burden). To a considerable extent, the ability to maintain a stable job and the ability to understand and learn are also affected (Fig. 1).

Although a significant percentage of the patients involved (81.25%) are in constant contact with the doctor, 37.5% of them consider that it is not enough for their needs. When it comes to tax cuts or reimbursement, more than 80% of patients feel that they are not supported enough. Patients evaluated benefits that they don't have access to based on their necessities (Table 1).

According to their response 50% of the patients who do not have access to specialized medical facilities consider it necessary for their care. Furthermore, we notice that 87.5% of patients do not receive professional psychological support, while 50% of them consider that they would need this support mechanism. Not all patients have access to financial aid. From this category 68.75% consider tax exemptions a necessity and 43.75% of them would need a stipend or other form of financial support. From the point of view of care, we notice that no patient studied considers that they received sufficient care in an interdisciplinary manner, adapted to the case.

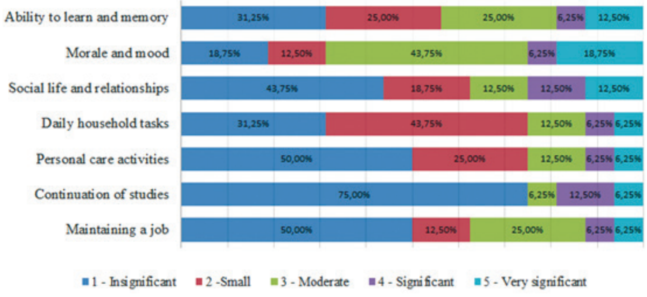

Figure 1. Daily life burdens for patients with REDs.

Patients were asked if they felt that at the time of diagnosis they had been provided with sufficient information from the attending physician regarding the disease and its management. The majority of patients (56%) did not consider that the information received at the beginning of the collaboration was sufficient, while 6% received no information on the disease and its management. The remaining 38% consider that the initial information was sufficient, but only half of them (19%) understood all the notions and medical terms. The sources from which patients constantly obtain information about the disease were also analyzed. From the survey respondents, 19% consider the healthcare professional the main source of information, 6% the patient organizations, 25% individual studies and 50% all of the above.

Medical education of endocrinologists in the field of RDs

The second group included 66 endocrinologists from Romania, of which 32 had the degree of primary doctors, 14 of specialist doctors and 20 of resident doctors. This group was also researched from the point of view of education on REDs and the main sources from which healthcare professionals obtain their information. In relation to the main sources from which doctors are informed about REDs, 71% of respondents consider international literature to be the main source of information, this percentage being followed by those who consider that continuing medical education events meet this purpose, representing 20% of respondents. Only 9% of doctors consider that the main source of information is formal education in the residency, while no doctor considers the information received during university studies or those received from patient associations as the main source of information. Only 48.5% of respondents state that the

Table 1. Benefits not considered sufficient by patients

Benefits insufficiently provided	Consider them necessary
Professional psychological assistance	50.00%
Help provided by social workers	18.75%
Assistance provided by phone or telemedicine	31.25%
Home healthcare	12.50%
Adequate access to the doctor	12.50%
Custom education and employment	25.00%
Tax exemptions	68.75%
Financial support or stipends	43.75%
Adequate medication or medical devices	18.75%
Access to specialised medical facilities	50.00%
Interdisciplinary medical care	37.50%

formal education they received in university or during residency is sufficient to treat patients suffering from these pathologies (47% consider it to be insufficient and 5% to be non-existent).

The physicians involved in the study were asked to assess their knowledge of important aspects in the management of endocrine BR (Fig. 2).

The aspect on which endocrinologists consider to have the most knowledge is the management protocols of patients with RDs, followed by the ability to provide genetic advice to patients. With regard to the rest of the aspects studied, most doctors consider that they have little or no knowledge of issues such as national registries for rare diseases, international reference networks, centers of expertise or the work of patient organizations. Only a very small percentage of doctors consider themselves experts in the following aspects: international reference networks (1.52%), centers of expertise for rare diseases (3.03%) or the activity of patient organizations (1.45%).

Both groups were asked if they had ever faced the situation in which the doctor did not know all the details about the RD that the patient suffers from and the latter provided that important information. Although the question was identical, the two groups have a different interpretation of the situations in which patients provide physicians with essential medical information. The majority of patients (75%) consider that at some point they provided important information to doctors when they did not have it. On the other hand, 61% of doctors don't consider that they have ever received such information from patients (Fig. 3).

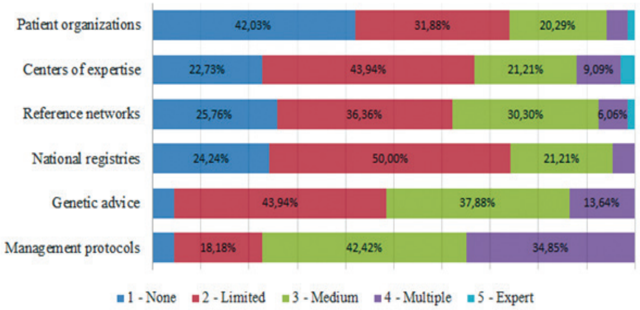

Figure 2. Endocrinologists' knowledge on important aspects in REDs management.

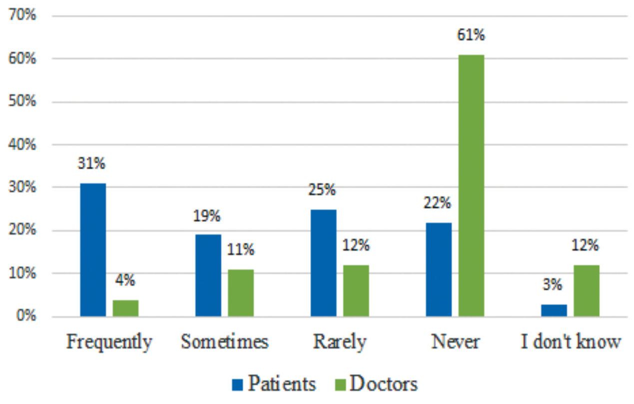

Figure 3. Perceived frequency of situations in which the doctor received important information on RDs from the patient, interpreted by both groups.

Involvement in research activities

Given the importance of medical research in improving the management of rare endocrine diseases, the two groups were asked about involvement of patients or POs in research activities (therapies, diagnostic methods, quality of life, etc.). Although 93,75% of patients and 86,40% of doctors consider patients should be involved in studies, out of the studied patients 69% have never been involved in a research activity (13% being involved in one project and 19% in two projects). Asked if they received enough information about projects and research opportunities, 75% of patients said they did not receive enough information, with the remaining 25% saying they did not have enough data to answer the question, while no patient included in the study considered to be sufficiently informed about involvement in research opportunities. When asked openly about the source from which they currently receive information about research opportunities, patients nominated organizations, the endocrinologists and individual study.

The two groups were questioned about issues that they consider in need to be improved in order to allow patients greater access to research opportunities. Most patients (44.1%) believe that better information is the solution. On the other hand, doctors almost equally believe that better funding, collaboration with patients' organizations, collaboration with researchers and better information are issues that need reform and improvement. An open question was addressed to doctors regarding the priorities for research into REDs, the most common answers being the following, with over 75% of subjects considering them important: development of therapies, development of diagnostic methods, improving patients' lives.

Impact of patient organizations

Both groups were asked about their membership or involvement in a patient organization, noting that 37, 56% of the patients are involved, while only 11% of the doctors are part of or collaborate with a PO (Fig. 4).

The patients and healthcare professionals were questioned about the importance of activities carried out by patient organizations in Romania. The perception was found to differ, for the patients surveyed most of the activities being considered to a very large extent essential, while the doctors gave less importance to the mentioned activities, considering them, to the greatest extent, important but not essential (Figs 5, 6).

In the final section of the questionnaire, both groups expressed openly their views on what they believe should be improved in the collaborative relationship between healthcare professionals and patient organizations. In the patient group, the following responses were the most common: creation of centers of expertise, in which doctors and patient representatives collaborate; increasing the involvement of doctors in POs; improving doctor-patient communication; including POs in more studies and public policies.

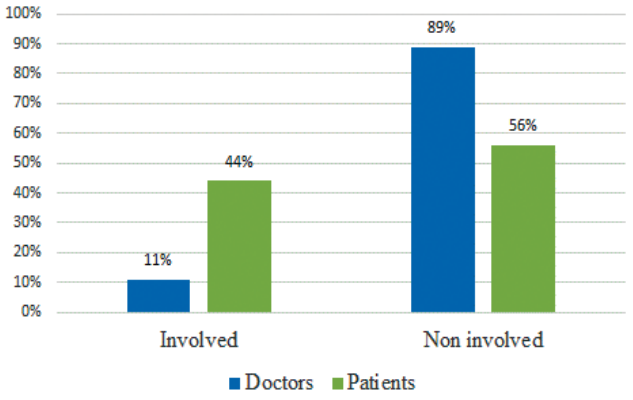

Figure 4. Involvement in patient organizations of doctors and patients.

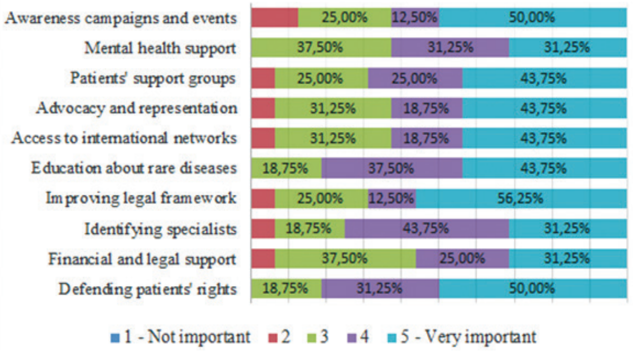

Figure 5. Assessment of the activity of POs in various sectors (Patients' view).

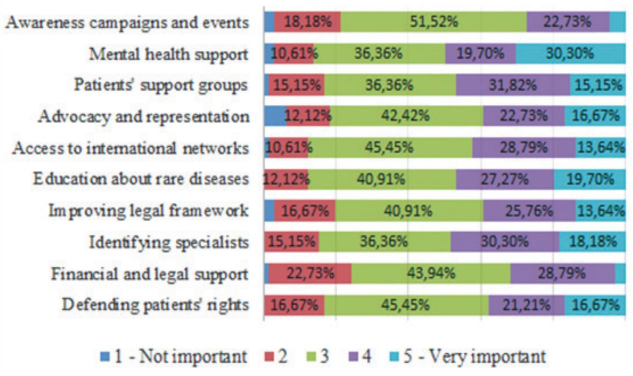

Figure 6. Assessment of the activity of POs in various sectors (Doctors' view).

The doctors surveyed had the following proposals: participation of patient organizations in continuing medical education events and more efficient promotion of their activity and needs among medical staff; conducting working groups or events through which the two entities communicate; establishing partnerships between hospitals or wards and POs relevant to them; mandatory referral of the patient to a dedicated organization after the diagnosis of rare endocrine disease; increasing the visibility of patient organizations and inviting physicians to join them.

DISCUSSION

This study assumed the role of providing initial data which can be used for development of a modern management plan for patients with rare endocrine diseases in Romania, which would provide concrete solutions to increase the quality of life for patients suffering from these pathologies.

Living with a rare condition is shown to cause hardships beyond medical symptoms, such as depression, lack of knowledge and uncertainty due to low prevalence [14]. After analyzing the results, mental health burden is confirmed to be a significant challenge in the lives of patients [15], alongside the lack of sufficient psychological support offered to these patients by the Romanian medical and social systems. Although the importance of integration in centers of expertise is recognized and documented nationally and internationally [16] to be very effective in care management and support of all kinds, we observe that patients consider them as insufficient and physicians do not possess the necessary knowledge about Romanian centers of expertise. Regarding patient support from authorities, patients consider three aspects to be essential for a better quality of life, but absent or insufficient at the moment in Romania: tax reductions, membership of a relevant center of expertise and professional psychological support. Though in many countries financial support is provided through social programmes to people with disabilities, patients with rare endocrine disorders don't necessarily fit into legal disabilities criteria. Patient organizations therefore have an opportunity to advocate to ensure that some of the socio-economic needs of such patients will be covered through special programmes. Given the high degree of impairment of individual and social quality of life in REDs, state or institutional support for these patients is essential for their full and effective integration into the community, the labor market, the education system or for full understanding of the care process [17].

In the case of rare diseases it is a common phenomenon for patients to specialize in their disease [18] and the medical education of healthcare professionals in rare diseases is an extremely complicated process due to the multitude of RDs and their diversity [19]. Therefore, it is interesting to note that Romanian patients consider themselves as a source of valuable information for doctors, while doctors have a contrasting opinion. When it comes to education of patients, according to the answers received, they do not consider that enough information was given by physicians at the time of diagnosis, but some of the specific communication needs of RDs patients [20] are covered by the availability of constant access to physicians. Physicians play an important role in constantly informing the patient, but we note that individual study and patient organizations should not be neglected, representing the main source of information for the patients.

The healthcare professionals' opinion regarding the insufficiency of formal education confirms the difficulty in specializing in the field of RDs, especially in countries that allocate few resources for the diagnosis and treatment of such disorders. But both patients and doctors consider that patient organizations play an important role in education, information and support processes, therefore POs could be the missing link, advocating for better education of healthcare workers on specific topics and informing patients about certain aspects of their condition.

Affirmative recognition of patients' roles in management of their disease should be advocated among both patients and physicians to facilitate an enhanced participation in care [21].

From the point of view of the scientific research process, unlike other diseases, rare pathologies are difficult to study. Studies, even those needed during the development of a drug, are extremely difficult to perform because a small number of patients are diagnosed and involved in this process. The main negative consequence of this is the difficulty of effectively identifying the side effects of orphan drugs, being important findings on the safety of these drugs [22, 23]. Patients with rare endocrine disorders have the right to fair treatment and distribution of means for research and development of medicines that will improve the quality of life of patients suffering from those diseases. In assessing the opinion of patients and physicians regarding research involvement in the field of RDs, most respondents did not have access to such an opportunity and consider that better information and collaboration with POs can increase involvement through financing, information and aggregation of interested individuals.

In conclusion, although the involvement of POs was considered important in all the studied aspects, we note that their activity is considered more important by patients, compared to the opinion of doctors involved in the study. These opinions are reflected in the involvement rate, a very small percentage of healthcare professionals collaborating with dedicated organizations in their activity. This reveals that although patient organizations have an important role in information, advocacy and support regarding rare diseases, there is a need to better inform healthcare workers about their activity and usefulness and in time incorporate those workers in POs activities increasing their reach and impact.

Patient organizations can be the key in providing better care to patients with rare disorders and it is necessary for similar research to continue in order to provide more data for decision makers and institutions involved in policy-making.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical Statement

The authors declare that all the procedures of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients and physicians included in the study.

Acknowledgment

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Study limitation

This study was conducted during the COVID-19 pandemic via an online questionnaire, filled mostly by patients from urban areas. To obtain more data, in further studies the survey should be distributed to patients in more regions, including rural areas.

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