Unveiling the hidden epidemic: Navigating orphan and rare diseases in healthcare



Rabin Debnath[1], Arshdeep Singh[1], Pooja A Chawla[2]*

[1]Department of Pharmaceutical Chemistry, ISF College of Pharmacy, G.T Road, Ghal Kalan, Moga, Punjab, 142001

[2]University Institute of Pharmaceutical Sciences and Research, Baba Farid University of Health Sciences, Faridkot, Punjab, 151203

Email: pvchawla@gmail.com

1 . Introduction

Orphan and rare diseases, often overlooked, impact a small proportion of the population, presenting unique challenges in diagnosis, treatment, and support. According to the Orphan Drug Act of 1983 in the United States of America, rare diseases impact fewer than 200,000 persons on average, but orphan diseases, according to the European Union (EU), affect fewer than 5 in 10,000 people (1). These illnesses cover a wide range, including genetic problems, some tumours, and autoimmune diseases. It is crucial to treat orphan and rare diseases for the benefit of both society at large and the afflicted individuals directly (2). Despite being uncommon, millions of people worldwide are impacted by orphan and rare diseases, which have a high morbidity and mortality rate. Due to their complex nature, many diseases require specialised attention and disproportionately affect vulnerable communities, exacerbating health inequities. Ignoring these problems hinders not only the quality of life of individuals and their families but also the progress of science and medicine (3). Orphan and rare diseases are a broad category of illnesses that are characterised by their rarity and often complex aetiology. Treatment and diagnosis of these conditions can be complex due to the way they impact several organ systems and create a wide range of symptoms. Orphan and rare diseases, the exact aetiology of which is yet unknown, are caused by a variety of reasons, including genetic alterations, environmental factors, and autoimmune dysregulation (4). Here, we look at a few distinct types of rare and orphan diseases (depicted in figure 1) and discuss their underlying causes:

1.1 Genetic disorders:

Duchenne muscular dystrophy, cystic fibrosis, and Huntington's disease are a few examples.

Cause: It is genetic mutations passed down from one or both parents, which lead to aberrant development or improper activity of certain genes or gene products. By interfering with vital biological processes, these mutations can result in a wide range of symptoms and outcomes (5).

1.2 Metabolic disorders:

PKU, Fabry disease, and Gaucher disease are a few instances.

Cause: Dysfunctions or imbalances in the metabolic pathways or enzymes that cause the breakdown or processing of certain substances, such as lipids, amino acids, or carbohydrates. The substances in question have the potential to build up within the body, resulting in harmful effects and tissue damage (6).

1.3 Autoimmune disorders:

Systemic lupus erythematosus (SLE), myasthenia gravis, and Sjögren's syndrome.

Cause: Dysregulation of the immune system results in the production of autoantibodies which attack and target healthy tissues and organs. The aetiology of autoimmune diseases is multifaceted and may involve immune system dysfunction, environmental triggers, and genetic susceptibilities (7).

1.4 Neurological disorders:

ALS, narcolepsy, and Rett syndrome are a few manifestations.

Cause: There are several factors that can lead to neurological issues, including imbalances in neurotransmitters, aberrant brain development, genetic mutations, and neurodegeneration.

Such circumstances often involve complex interactions involving genetic and environmental factors (8).

1.5 Rare cancers:

Cholangiocarcinoma, pancreatic neuroendocrine tumours, and mesothelioma are a few instances.

Cause: Unusual cancers tend to be more common or are brought on by specific genetic mutations or environmental exposures, despite the fact that smoking, radiation exposure, genetic predisposition, and other known risk factors are linked to a high risk of cancer. To enhance outcomes and develop targeted treatments, it is imperative to understand the underlying causes of rare malignancies (9).

1.6 Infectious diseases:

Lassa fever, Ebola virus sickness, and Creutzfeldt-Jakob disease are among them.

Cause: Infections with uncommon pathogens such prions, certain viruses, or bacteria can result in rare infectious illnesses. Such infections could only take place in specific locations where the bacteria are endemic (10).

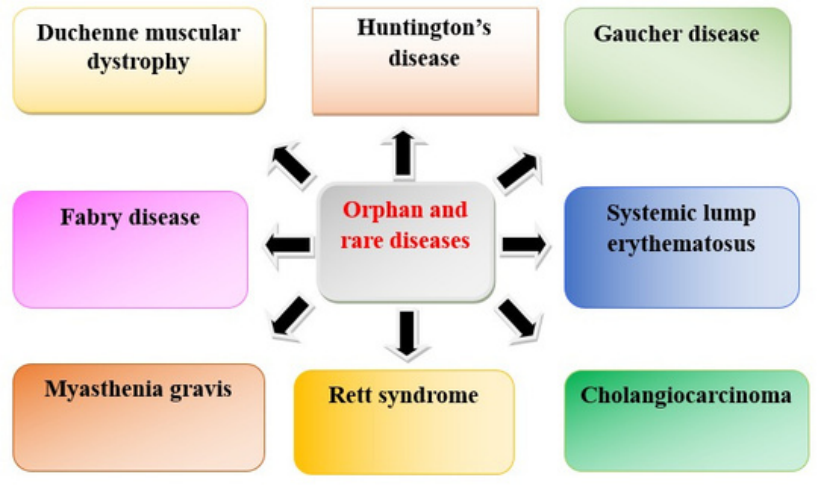

Figure 1. Some examples of orphan and rare diseases

2. Recognising rare and orphan diseases

A vast range of illnesses are included in the category of orphan and rare diseases, all of which are connected by the fact that they only afflict a small portion of the population. These illnesses are often distinguished by their infrequency, intricacy, and difficulties in diagnosis, treatment, and research. A number of important factors are involved in determining which diseases are orphan or rare:

2.1 Genetic basis

Numerous orphan and rare diseases can be caused by chromosomal abnormalities, mutations, or changes in specific genes. These genetic abnormalities can trigger a variety of clinical symptoms by messing with normal cellular functions (11).

2.2 Global impacts

Millions of individuals worldwide suffer from orphan and rare diseases, which are uncommon in and of oneself, affecting all ages, genders, and ethnicities. The stress that patients and their relatives experience from these illnesses is increased by the absence of adequate research funding and appropriate treatments. In addition to having a huge financial burden on society and healthcare systems, many illnesses cause terrible mental and physical pain for those who are affected (12). The fight against these requires increased public awareness, international cooperation, and advocacy for better research funding, diagnostic tools, and easier access to specialised treatment and therapies. By raising consciousness regarding orphan and rare diseases, we may work to improve the lives of individuals affected and advance research towards more effective therapies and treatments (13).

3. Difficulties in diagnosis and therapy

Monitoring rare and orphan diseases involves navigating a complex network of challenges, from the initial stages of diagnosis to ongoing treatment for these sometimes-fatal illnesses. The primary reason for these issues is the general lack of knowledge concerning orphan and rare diseases that permeates society, the healthcare system, and even the ranks of medical professionals. Due to their rarity and low visibility, many rare diseases remain poorly recognised or go undiagnosed, which results in significant delays before treatment can begin. Patients frequently find themselves in the middle of a painful and lengthy diagnostic process that involves visiting several different medical specialists and undergoing a battery of tests in order to get a precise diagnosis. This procedure frequently results in incorrect diagnoses, which stresses out patients and their families and produces therapies that don't work (14). Getting access to expert care and treatment is also one of the largest difficulties encountered by those with rare and orphan diseases. Treating these problems occasionally calls for interdisciplinary teams of experts, including pulmonologists, neurologists, geneticists, and others. However, there are situations when it is difficult to obtain this knowledge, particularly in poor or rural locations where treatment resources may be limited. The expense and availability of specialised diagnostic an procedures, therapies, and medications may also provide insurmountable challenges for a large number of patients, aggravating care inequalities and maintaining structural inequity in the healthcare system. A thorough and coordinated effort must be made on multiple fronts to address these complicated difficulties. Increasing public awareness of orphan and unusual illnesses and its policymakers' and healthcare professionals' understanding of them is essential to improving early recognition and diagnosis (13).

4. Prospects for the future and difficulties

Despite several challenges, there have been significant advancements in the field of orphan and rare illness studies that offer hope for the future. Advancement in precision medicine, computational biology, and genomics is transforming our knowledge of uncommon diseases. Researchers may now identify novel genetic variants, elucidate disease pathways, and create specialised treatments thanks to these advancements (4). Further encouraging innovation in rare illness research and drug development, expediting research findings, and facilitating data exchange are the growing collaborations among scientists, patient advocacy groups, industry partners, and governmental agencies However, numerous additional obstacles need to be , addressed before orphan and uncommon diseases can be fully treated (15). Lack of funding for research, uneven access to medicines and care, diagnosis delays, and the high cost of creating orphan pharmaceuticals are some of these challenges. Individualised approaches and customised treatment regimens are essential, as the variety of uncommon diseases poses significant obstacles to the production of efficient medicines that can help every patient (13). To solve these difficulties a financing and persistent collaboration from a range of sectors including government, business, academia, and patient advocacy groups will be required. Additional

cooperation and funding are needed to progress research, improve diagnostic capabilities, expand access to care and medications, and ultimately improve outcomes for patients with rare and orphan diseases. By working together to achieve common goals and making use of our collective expertise and resources, we can overcome the remaining challenges and pave the way for a better future for those with orphan and uncommon illnesses (15).

5. Conclusion

In order to sum up, fighting orphan and rare diseases necessitates concerted efforts to overcome challenges and benefit from new advancements in collaboration and research. Important challenges involve the necessity for continuous cooperation and funding in addition to the developments in genomics and precision medicine. Limited resources and uneven access are further issues. It is essential that we put out a call to action for increased awareness and support, pleading with interested parties to demand improved funding for healthcare access, education, and research. Working together and prioritising the needs of persons with rare and orphan diseases can greatly enhance results and standard of life.

References

1. Shashel VA, Firsova VN, Trubilina MM, Podporina LA, Firsov NA. Orphan diseases and associated problems. Medical Herald of the South of Russia. 2021 Jul 4;12(2):28-35.
2. Fermaglich LJ, Miller KL. A comprehensive study of the rare diseases and conditions targeted by orphan drug designations and approvals over the forty years of the Orphan Drug Act. Orphanet Journal of Rare Diseases. 2023 Jun 23;18(1):163.
3. Rajtar M. The Pre-Existing Vulnerabilities of Patients With Rare Disorders in Poland During a Global Pandemic (#WitnessingCorona). Medizinethnologie Körper, Gesundheit und Heilung in einerglobalisierten Welt. 2020;6:2020.
4. Richter T, Nestler-Parr S, Babela R, Khan ZM, Tesoro T, Molsen E, Hughes DA. Rare disease terminology and definitions—a systematic global review: report of the ISPOR rare disease special interest group. Value in health. 2015 Sep 1;18(6):906-14..
5. Boycott KM, Vanstone MR, Bulman DE, MacKenzie AE. Rare-disease genetics in the era of next-generation sequencing: discovery to translation. Nature Reviews Genetics. 2013 Oct;14(10):681-91..
6. Özer I. New Treatment Options in Rare Diseases. Journal of Pharmacy and Pharmacology. 2021 Nov 25;9:273-7.
7. Lee DS, Rojas OL, Gommerman JL. B cell depletion therapies in autoimmune disease: advances and mechanistic insights. Nature reviews Drug discovery. 2021 Mar;20(3):179-99.
8. Shah S, Dooms MM, Amaral-Garcia S, Igoillo-Esteve M. Current drug repurposing strategies for rare neurodegenerative disorders. Frontiers in pharmacology. 2021 Dec 21;12:768023.
9. Mittra A, Takebe N, Florou V, Chen AP, Naqash AR. The emerging landscape of immune checkpoint inhibitor based clinical trials in adults with advanced rare tumors. Human Vaccines &Immunotherapeutics. 2021 Jul 3;17(7):1935-9.
10. Alrakah DM, Alyami YS, Alyami AR, Aljearah HA, Al Okeel NH, Al Swaidan MH, Mershed MA, Al Ageil MH, Alyami NH, Alhareth AS, Al Yami HM. Prevention of Blood-borne Infections in Hospital Settings. Advance in Clinical and Experimental Medicine. 2023;10(1).
11. Ramos-Fuentes F, González-Meneses A, Ars E, Hernández-Jaras J. Genetic diagnosis of rare diseases: past and present. Advances in therapy. 2020 May;37:29-37.
12. Collin-Histed T, Gershkowitz J, Stevens B, Timmins G. The Patient Perspective on Rare Diseases. Lysosomal Storage Disorders: A Practical Guide. 2022 Jul 21:299-307.
13. Belousova OA, Groen AJ, Ouendag AM. Opportunities and barriers for innovation and entrepreneurship in orphan drug development. Technological Forecasting and Social Change. 2020 Dec 1;161:120333.
14. Denton N, Mulberg AE, Molloy M, Charleston S, Fajgenbaum DC, Marsh ED, Howard P. Sharing is caring: a call for a new era of rare disease research and development. Orphanet Journal of Rare Diseases. 2022 Oct 27;17(1):389.
15. Groft SC, Posada M, Taruscio D. Progress, challenges and global approaches to rare diseases. Acta paediatrica. 2021 Oct;110(10):2711-6.