Document No. STI-FF/03/2023

# A Fact File on
# RARE DISEASES
## An Emerging Global Health Priority

(A Joint Publication of the NAM S&T Centre and JSS Medical College, JSS Academy of Higher Education & Research, Mysuru, India)

## FROM THE DG'S DESK

Warmest Greetings to all our Esteemed Readers!

I am happy to present before you a new Fact File titled "**Rare Diseases: An Emerging Global Health Priority**".

A Rare Disease affects only a smaller percentage of the population, compared to other general diseases. Its prevalence is comparatively very low. As rare disease occurs infrequently in a population, there is no universal definition. The World Health Organization (WHO) defines a rare disease as an often debilitating lifelong disease or disorder condition with a prevalence of 1 or less, per 1000 population. It is estimated that there are about 7000 rare diseases. Most of the rare diseases – (about 80%) are genetic and hence affects a large number of children. Some rare diseases are not inherited such as – some rare cancers, auto-immune diseases, infectious tropical diseases, etc. Unfortunately, there are no treatments available for many rare diseases. Identification and treatment of rare diseases is a challenging task because of the general lack of awareness and very limited availability of scientific and medical infrastructure.

It is thus essential for medical community, healthcare practitioners, researchers, experts, professionals and other international stakeholders across NAM Member and other developing countries to work cohesively with WHO, health-system managers and policymakers in designing their national level policy and building capacity for treatment of rare diseases.

Amitava Bandopadhyay

**(Amitava Bandopadhyay)**

### Introduction

Rare Diseases (RDs) affect a relatively small proportion of the world's population; although individually, these disorders are uncommon, collectively, they account for a significant number. Every country has its own definition and criteria for rare diseases; hence, there is no single widely accepted definition of it. Due to different criteria for the definitions and challenges with data collection, estimates of the total number of RDs vary across countries and studies. It is estimated that 80% of RDs are genetic in origin. There is a lack of data, evidence and knowledge about RDs due to their inherent heterogeneity, complexity and low patient numbers.

### Global Scenario of RDs

Globally, rare diseases are emerging as important public-health concerns. According to the World Health Organization (WHO), incidence of rare diseases is estimated to be less than 6.5 per 10,000 population. While there is no universal definition of RD, some consider the number of people diagnosed with a particular disease, while others include the availability of adequate treatments or the severity of the disease. Some of the countries have also included rare bacterial and viral infections, allergies, and even degenerative diseases in the list.

The table 1 and 2 depicts the definition of RDs in some of the NAM and Non NAM countries.

**Table 1: Country Definitions of Rare Diseases according to NAM Regions**

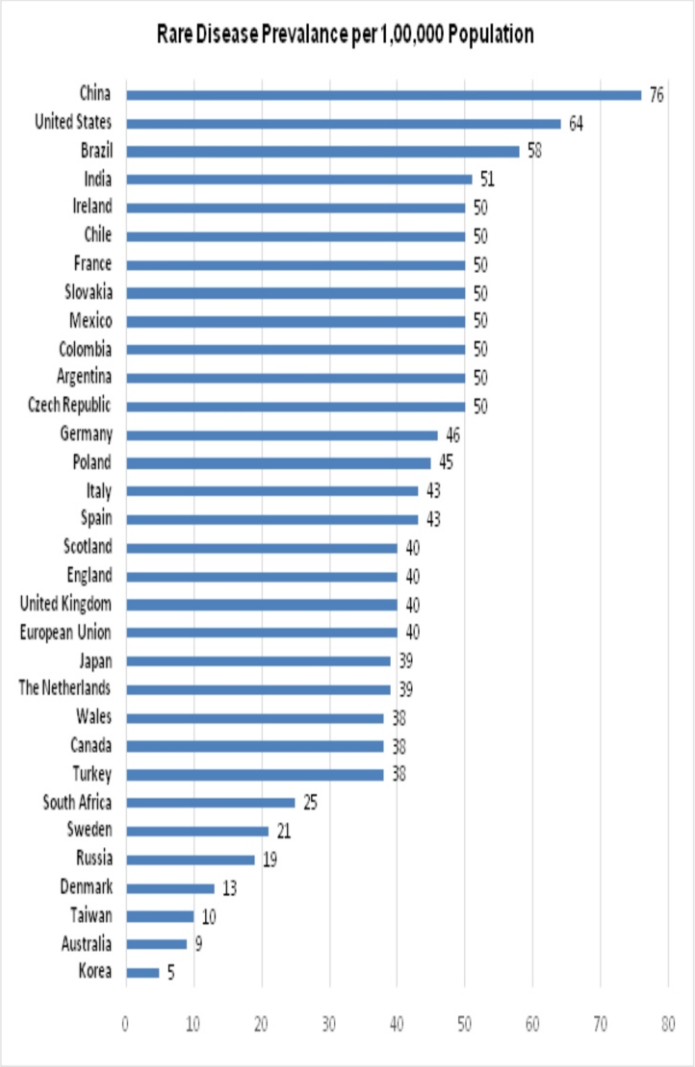
| COUNTRY | FIXED NUMBER OF PATIENTS | PATIENTS PER 100,000 |
|---|---|---|
| **Africa: Out of 53 NAM countries in this region only South Africa has defined rare diseases** | | |
| South Africa | | 25 per 10000 population |
| **Asia: Out of 39 Asian countries in NAM, none has defined rare diseases** | | |
| **Latin America and Caribbean: Out of 26 countries in this region five countries have defined the rare diseases** | | |
| Panama | -- | Less than 50 per 100000 population |
| Mexico (Observer country) | -- | Less than 50 per 100000 population |
| Chilie | -- | Less than 50 per 100000 population |
| Colombia | -- | Less than 50 per 100000 population |
| Peru | -- | Less 1 in 100,000 |
| **Europe: Out of two European countries in NAM, both have no definition of rare diseases** | | |

**Contributing Authors:** *Deepa Bhat, Akila Prashant, Basavanagowdappa Hathur, Praveen Kulkarni, JSS Medical College,JSS Academy of Higher Education & Research, Mysuru*

**Table 2: Definition of Rare Diseases in other Countries/Regions which are not in NAM Countries**

| Country | Patients per 100,000 |
|---|---|
| United States | 61 in 100,000 |
| Europe | 50 in 100,000 |
| Australia | 50 in 100,000 |
| China | 76 per 10,000 people |
| Russian Federation | 10 in 100,000 |
| Brazil | 65 in 100,000 |

*Source: (https://www.keionline.org/wp-content/uploads/KEI-Briefing-Note-2020-4-Defining-Rare-Diseases.pdf)*




*Adapted from Richter T et al.; International Society for Pharmacoeconomics and Outcomes Research Rare Disease Special Interest Group. Rare Disease Terminology and Definitions-A Systematic Global Review: Report of the ISPOR Rare Disease Special Interest Group. Value Health. 2015 Sep;18(6):906-14.*

The above two depictions highlight the fact that there do not exist the common accepted definition for RDs.

By and large, the RDs include inherited cancers, autoimmune disorders, congenital malformations, neuro-degenerative disorders, rare infectious diseases, haemangiomas, hirschsprung disease, gaucher disease, cystic fibrosis, muscular dystrophies, and lysosomal storage disorders (Inborn errors of metabolism)

**Table 3: Some of the Rare Disease List from different Networks and Countries**

| | | |
|---|---|---|
| Acanthocytosis Chorea | Glandular Cheilitis | Nephropathic Cystinosis |
| Achalasia Cardia | Gluten Ataxia | Neurofibromatosis |
| Acromesomelic Dysplasia | Goodpastue Syndrome | Niemann Pick Syndrome |
| Acute LympoblasticLukemea | Guillain Barre Syndrome | Nodular Prurigo |
| Adrenoleukodystrophy(ALD) | Haemangioma | Oculodentodigital Syndrome |
| Alkaptonuria | Hajdu-Cheney Syndrome | Osteogenesis Imperfecta |
| Amyotrophic Lateral Sclerosis | Hallermann-Streiff syndrome | Pachydermoperiostosis |
| Apert Syndrome | Hereditary Spastic Paraplegia | Pemphigus Vulgaris |
| ATAXIA TELANGIECTASIA | Hirschsprung's disease | Pfieffer Syndrome |
| Aplastic anaemia | Hunter Syndrome | Phenylketonuria |
| Batten Diseases | Hydrocephalus | Pierre Robin Syndrome |
| Becker's Nevus. | Inborn errors of metabolism | Prader Willi Syndrome |
| Bilateral Anorchia | Interstitial Cystitis | Progeria |
| Biotinidase Deficiency | ITP | Retinitis Pigmentosa |
| Budd Chiari Syndrome | Johanson Blizzard Syndrome | Robinow Syndrome |
| CANAVAN DISEASE | Joubert Syndrome | Scleroderma |
| Cartilage Hair Hypoplasia | Kabuki Syndrome | Spinocerebellar Ataxias |
| Cerebellar Ataxia | Kleeftra Syndrome | Spodylocostal Dysostosis |
| Chaple Syndrome | Klinefelter Syndrome | Steven Johnson Syndrome |
| Charcot Marie Tooth | Lamellar Ichthyosis | Sturge Weber Syndrome |
| Charcot-Marie-Tooth Disorder | Leigh syndrome | SLE |
| Criggler Najjar Syndrome | Lennox Gastaut Syndrome | Tay Sachs Disease |
| Cystic Fibrosis | Lion Face Syndrome | Torg - Winchester Syndrome |
| Dense Deposit Disease | Lipid Storage Disease | Transverse Myelitis |
| Diastrophic Dysplasia | Lupus Nephritis | Tuberous Sclerosis |
| Dysferlinopathy | Lysosomal Storage Disorders | Torg - Winchester Syndrome |
| Ectodermal Dysplasia(ED) | Maple Syrup Urine Disease | Tarlov Cyst |
| Fabry Disease | Marcus Gunn Syndrome | Usher Syndrome |
| Farber Disease | Maroteaux-Lamy Syndrome | Vitiligo |
| Fibromylagia | Melnickneedles Syndrome | Von Hippellindau Syndrome |
| Fibrous Dyslapsia | Menière Disease | Vitiligo |
| Friedreich's Ataxia | Menkey Kinky Hair Disease | Warburg Micro Syndrome |
| Friedreich's Ataxia | Mitochondrial disorders | Wilson Disease |
| Gaucher Disease | Motor Neurone Disease | Wolfram Syndrome |

More detailed lists of rare diseases in different countries and networks are available in the following links.

- https://www.morganlewis.com /-/media/ files/ pubs/china_raredisease_list.ashx ?
- https://rarediseases.org/rare-diseases/
- https://rarediseases.info.nih.gov/diseases?category= &page=1&letter=& search=
- www.orpha.net
- https://ordindia.in/about-rd/rare-disease-in-india/
- www.omim.org

The National Institutes of Health (NIH) estimates that between 25 and 30 million Americans suffer from RDs and among them two third are children. A database of approximately 1,300 reports on specific rare diseases is available on the website of the National Organization for Rare Disorders (NORD) and NIH Genetic and Rare Diseases Information Center (GARD) website has the most comprehensive listing of rare diseases in the U.S. It is the leading nonprofit initiative representing all patients and families with rare diseases in the United States. Established in the year 1983, NORD is the country's largest rare disease organization which works towards identification, treatment and cure of all 7,000 RDs in United States.

The European Union defines rare diseases (RDs) as life threatening or chronically debilitating conditions whose prevalence is less than 5 per 10,000. More than 8000 rare diseases or groups of diseases affecting between 6% and 8% of the European people are described in the Orphanet database. The Orphanet network (www.orpha.net) is a 37-country network funded by the European Commission that aims to improve diagnosis, care and treatment of RDs. In other words, between 27 and 36 million persons in the European Union are affected by rare diseases. In April 2007, the WHO established Topic Advisory Groups (TAGs) for RDs. Orphanet has developed a strictly clinical in-house classification to meet clinician needs and serve as a basis for building the ICD-11 revision.

The European Joint Programme – Rare Diseases (EJP-RD) is another inclusive effort to build on existing resources, experiences and networks including eRare, Orphanet, RD-Connect, EURORDIS, ERNs, and research infrastructures like ELIXIR (www.elixir-europe.org), BBMRI (www.bbmri-eric.eu), EATRIS (https://eatris.eu/), ECRIN (www.ecrin.org), INFRAFRONTIER (www.infrafrontier.eu), amongst many others that allows high-level strategic organization and performance of research activities in an organized manner.

**Managing RDs through International Collaboration**

A global collaboration between the European Commission and the National Institutes of Health, the International Rare Diseases Research Consortium (IRDiRC) was established in 2011 with the goal of tackling rare diseases through research. Achieving the vision to provide accurate diagnosis, care and available therapy to all people living with rare diseases within one year of seeking medical attention is the objective of IRDiRC. Currently, the Consortium has 60 member organizations on all continents. It works towards advancing diagnostics and treatments and understanding the impact these have on people living with rare diseases. Individually, some of the countries have a specific group working towards the RDs. In Canada, for example, the initiative Care4Rare connects 21 academic sites to a team of collaborating clinicians, researchers, scientists and bioinformaticians who work on improving the diagnosis. In Europe, EURenOmics and NeurOmics consortium are the collaborative research network of about 100 clinicians and researchers from ten countries to advance research.

**Status of Rare Diseases in Developing Countries**

Information about RDs is limited in low- and middle-income countries (LMICs). This suggests that patients from these countries may be missing from global databases and reports. The awareness of RDs in these countries is low, and little is known about them. There is a lack of data on the types of diseases, their incidence, distribution and numbers

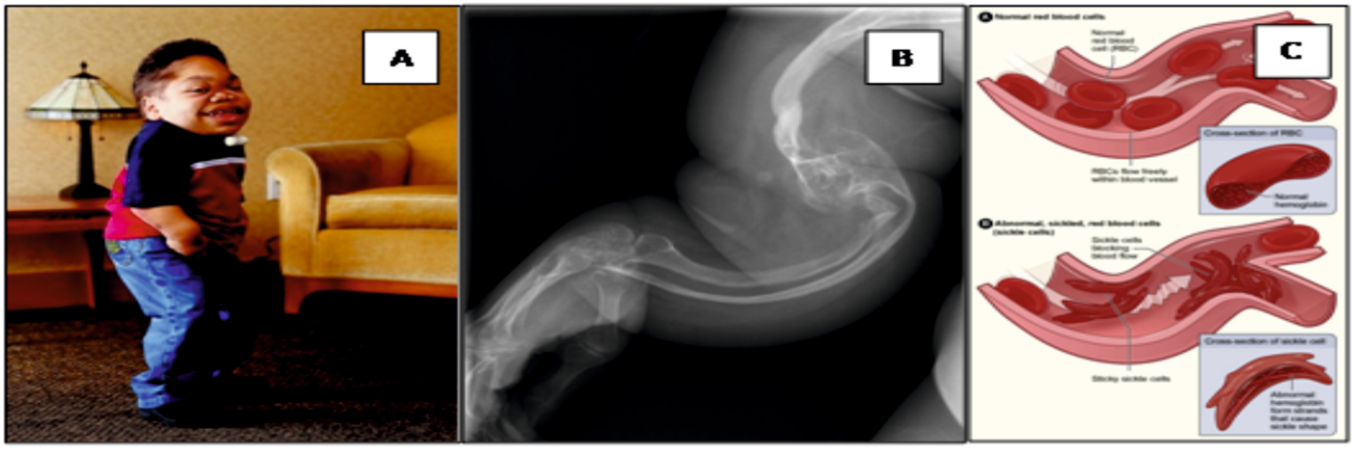



**Figure 1. A.** Mucopolysaccharidosis Type 1 **B.** X Ray in Osteogenesis Imperfecta **C.** Sickle Cell Disease *[Source: Wikipedia]*

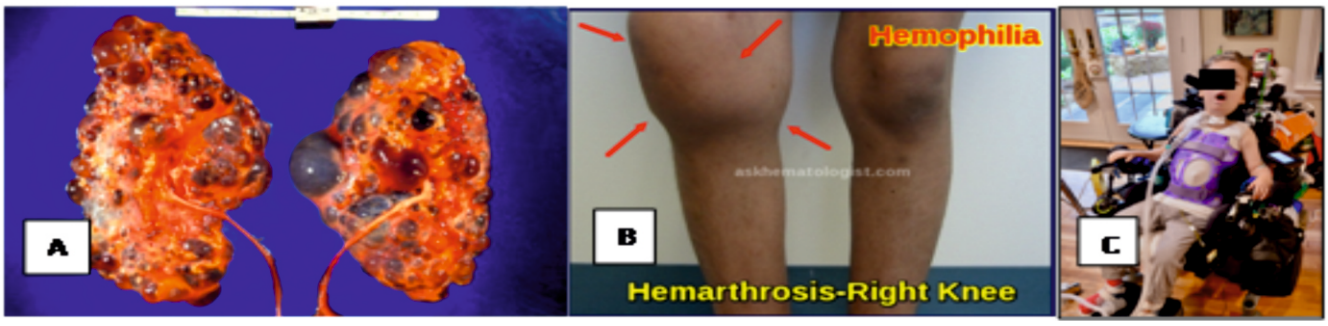



**Figure 2. A.** Polycystic Kidney disease **B.** Joint bleeding in haemophilia **C.** Spinal Muscular Atrophy *[Source: "Polycystic kidney disease". MedlinePlus Medical Encyclopedia. Retrieved 2015-07-30. Joint Bleeds and Hemophilia | Preventing Joint Damage (ihtc.org)]*

of the affected individuals. Additionally, the struggle to detect RDs, missed and delayed diagnosis has led to poor treatment of these conditions.

In Africa, genomic research is still struggling with ethical issues, including genomics literacy, good governance, privacy protection, and the protection of the public and the data. During the 11th International Conference on Rare Diseases (ICORD), stakeholders from the national, African continental, and international levels met in Cape Town, South Africa, to launch the Africa-Rare initiative. It focuses on improving awareness of rare diseases, enhancing access to diagnosis, treatment, supportive care and research, as well as developing policies related to rare diseases in African countries. Another group called "Rare Disease Working Group" comprising of the delegates from H3Africa-funded projects work within the rare genetic disorder niche. Their research initiatives are aimed at identifying and filling the knowledge gaps in rare disease in Africa by characterizing the clinical and molecular epidemiology of specific groups of rare diseases, including developmental delay, deafness, neurodegenerative and neuromuscular diseases. In Tanzania, a "Call for Action" focused on seventeen items to lay a firm foundation for infrastructure, policies and guidelines to improve management of RDs and potentially contribute to reducing the burden on individuals with RDs and their caretakers/ families has been proposed recently.

In Southeast Asia, there is a considerable difference in the RD initiatives across countries based on the economic status. The countries like Philippines, Singapore, Malaysia, Indonesia, Vietnam and Thailand although has fairly developed national health programmes but they are far behind best practice countries like Taiwan and South Korea in terms of RDs as a public health priority.

Like many other developing countries, India also lacks a standard definition for Rare Disease. The country being the most populous in the world, the Organisation for Rare Diseases India (ORDI) recommends designating a disease as rare if it affects lesser than 5,000 people by a particular disease. About 80% of RDs in India are genetic, with many being monogenic in inheritance. Approximately half of them may manifest at birth and the rest later in life, with variable severity. About 450 RDs have been reported from tertiary care hospitals in India. The most common RDs observed in India are haemophilia, thalassemia, sickle cell anaemia, primary immuno-deficiency disorder in children, auto-immune diseases, lysosomal storage disorders, cystic fibrosis, haemangiomas, and certain forms of muscular dystrophies etc. Several Non-Government Organisations (NGOs) and disease specific patient advocacy groups are working towards RD. ORDI is a section 25 non-profit organization representing the collective voice of all Indian patients with rare diseases to promote Rare Diseases as human rights priority through public awareness. They work towards the development of Public Policy and take part in implementation, such as Rare Disease Policy and Orphan Drug Policy, collaborate with advocacy organizations from India, and abroad, accelerate diagnosis and treatment options for patients with rare diseases through public-private partnerships, facilitate Clinical Trials, Research and Orphan drug development activities. Many such disease specific groups, such as Cure-SMA, MERD India and Lysosomal Storage Disorders Support Society etc, work towards similar causes and provide assistance to the RD community.

Some of the RDs are represented in figure nos. 1 and 2.

**National Policy for Rare Disease (NPRD) in India**

Ministry of Health and Family Welfare, Government of India formulated a National Policy for Treatment of Rare Diseases (NPTRD) in July, 2017. The policy was further renamed as National Policy for Rare Diseases (NPRD) and launched in March 2021. The salient features of NPRD, 2021 are as follows:

The Rare Diseases have been identified and categorized into 3 groups namely:

**Group 1:** Disorders amenable to one-time curative treatment. Ex: Hematopoietic Stem Cell Transplantation (HSCT) or organ transplantation.

**Group-2:** Diseases requiring long-term/lifelong treatment ex: special dietary formulae or other forms of therapy.

**Group 3:** Diseases for which definitive treatment is available but challenges are high cost and lifelong therapy.

8 Centres of Excellence (CoEs) have been identified for the diagnosis, prevention and treatment of rare diseases and 5 Nidan Kendras have been set-up for genetic testing and counselling services outside of the Rastriya Arogya Nidhi Umbrella Scheme. The complete details of the policy are available at

https://rarediseases.mohfw.gov.in/uploads/Content/1624967837_Final-NPRD-2021.pdf

**Orphan Drugs and Act**

In 1983, the United States passed the Orphan Drug Act to facilitate the development of drugs to treat rare diseases. A drug that is designated as an orphan drug does not imply that it is safe, effective or that it is legal to manufacture and market it. However, this indicates that the sponsor qualifies for benefits from the federal government including market exclusivity and tax reductions. Due to low returns on investment, industries show little interest in developing treatments for rare diseases. There is a strong dependence on government incentives for the development of orphan drugs. Protocol assistance, fast-track approval, waiver of fees and marketing exclusivity are some of the benefits offered by many countries, such as the USA, Japan, etc. However, India is still in the developing phase, there is a setback regarding regulation and development in orphan diseases research. "The New Drugs and Clinical Trial Rules 2019" define an orphan drug as one that treats a condition that affects fewer than five lakh (500,000) Indians. Orphan Drug clinical trials follow the same regulatory framework as other drugs, with the following exemptions:

- In cases of orphan drugs, the highest drug regulatory organization in India, the Central Drugs Control Standards Organization (CDSCO) can waive the requirement of local clinical trials.
- Clinical trial sponsors for orphan drugs may ask the CDSCO to expedite the approval process.
- It is not necessary to pay an application fee for a clinical trial of an orphan drug.

**Public Health Impacts due to RDs**

Rare Diseases are found to have multidimensional impact on individuals, families and communities. The disabilities arising from the disease manifestations, its diagnostic and treatment uncertainty have a detrimental influence on the health, psychosocial, and economic wellbeing of individuals and families of patients with rare diseases.

Additionally, there is a lack of awareness among general public and health professionals on the burden, manifestations, diagnosis, treatment and consequences of rare diseases. Rare diseases have also sought considerably negligible attention from health systems and policymakers.

**Economic Burden due to RDs**

RDs pose considerable economic burden to the families and communities. The direct costs incriminated to the RDs are associated with hospital inpatient care, diagnosis and medications. Indirect costs primarily related to sickness absenteeism and early retirement. The scale of RDs economic burden requires immediate attention from scientific communities, policymakers and other key stakeholders such as health care providers and employers. There is a need to think innovatively and collaboratively to identify new ways to improve the care, management and treatment of these often-devastating diseases.

**Challenges in RDs**

There is a significant challenge associated with diagnosing and treating rare diseases (RD). The US (1983) and EU (2000) passed legislation aimed at reversing the previous neglect of RD by providing incentives for the development of orphan drugs (ODs). There are several challenges associated with diagnosis, treatment, and reporting of rare diseases.

**1) Timely Diagnosis**

- Clinical presentation of most of the rare diseases are similar in several common illness, thus posing difficulty in timely diagnosis
- Lack of awareness among doctors and the health care system about the clinical presentations of RDs
- Underlying molecular or physiologic mechanisms are unknown in many
- Dearth in the number of medical geneticists and genetic counsellors catering to the National Population
- Facilities for laboratory diagnosis are available only in metropolitan cities

**2) Lack of Knowledge and Awareness** among public as well as health care provides about the manifestations, diagnosis, consequences, treatment and prevention of rare diseases.

**3) Reporting**

- Direct to consumer availability (DTC): Direct availability of testing opportunities for the consumers
- Incomplete understanding about the choice of test
- Scope and capacity of most registries and databases are limited
- Complete understanding of gene causation not yet available
- Screening strategies lack efficiency
- Cost of investigation and management
- Lack of National Registries

**4) Orphan Drug Designation and Treatment for RDs**. Apart from the public health concerns RD have characteristics that present serious challenges for health practitioners.

- Standards of care for treatment and rehabilitation are not evidence-based because health research is done at small scale
- Very few RDs are curable and the cost of the same is exorbitant
- Absence of insurance coverage
- No universal policy on orphan drugs

**Crucial Role of the Genetic Counselling in Rare Diseases**

The diagnosis of RDs (either clinically, genetically, or both) is not the end of the journey for patients and their families. It is very important to understand the disease, manifestations and adaptation to life with an affected individual after genetic confirmation. To avoid the birth of the affected, the disease should also be tested within the family to prevent the disease from passing on. Rare disorders may also occur de novo, with the patient being the first member of the family to be affected by these disease-causing genetic changes. Genetic counselling involves communicating with people about how genetic variants affect their lives and health, as well as adapting to the medical, psychological and familial effects of genetic disorders.

**Roadmap for the Prevention & Control of Rare Diseases:**

a) **Raising public awareness:** Public awareness on RDs must be enhanced through focused health awareness programs and behaviour change strategies. The public awareness activities should concentrate on the hereditary basis of rare diseases and the time at which it is appropriate to seek medical care.

b) **Strengthening preventive measures:** As only a handful of rare diseases have cures, which are also exorbitantly priced, prevention is the best option. Birth of child with rare diseases can be prevented through primary preventive measures like prospective and retrospective genetic counselling. Despite not always being feasible, this strategy has the highest yield when it comes to reducing the prevalence and incidence of rare disorders. In secondary prevention, the aim is to prevent the birth of affected foetuses (prenatal screening and prenatal diagnosis), to detect and treat disorders early (early detection), and to minimize the manifestations of the disorders thereafter (newborn screening). The tertiary prevention strategies include provision of better care and medical rehabilitation to patients suffering from rare diseases who are at an advanced stage of their illness. The goal is to improve the quality of life of patients with various rare disorders, including those for which there is no specific treatment.

c) **Capacity building of healthcare-system:** Genetic diseases exhibit the same symptoms as other diseases. Hence during clinical evaluation, they are considered as unlikely differentials. There is a need to enhance the knowledge and skills of doctors and health care workers on clinical presentations, diagnostic modalities, treatment options and prevention of rate diseases. Patients and healthcare providers would benefit from a hub and spoke model connecting primary health to centres of excellence in diagnosis and management of rare diseases.

d) **Screening and diagnosis:** Considering the need for sophisticated lab infrastructure, cost of diagnostics and larger population sizes, screening of every pregnancy for the rare diseases is not a feasible and viable option in low-and-middle-income countries. To address the burden, an algorithm should be developed and implemented which will be appropriate to the socio-economic status of population and geographical location.

e) **National RDs Registry:** There is a need for a single registry that documents RDs across the nation and all the countries with standard operating procedures for regular updates. The RDs community would suffer if there are multiple parallel groups working for the same cause. There is a need to establish National Registry to collect RDs data and monitor clinical outcomes.

## Conclusion

Rare Diseases are emerging out to be major public health concerns across the world. There is need for global health concern and a national policy priority. Considering the wide variations in definitions, clinical presentations, lack of awareness among health care providers and under reporting of cases, the actual magnitude of the rare diseases is yet to be explored. Enhanced screening and cost-effective diagnostic activities through scientifically sound methods and technologies may help in exploring the hidden portion of the iceberg and help in excluding few diseases from the list of rare diseases. There is a need to adapt focused measures in raising the public awareness, empowering the healthcare providers on diagnosis, management and prevention of rare diseases. It is essential that the international stakeholders from countries of the Non-Aligned Movement (NAM) and the World Health Organisation (WHO) work cohesively with national level policymakers in designing the country specific strategies in reducing the burden of rare diseases.

## References


1. Organization for Rare Diseases in India. Weblink available from URL https://ordindia.in/about-rd/rare-disease-definition/ retrieved on05.09.2023, 11.00 IST
2. Ferreira CR. The burden of rare diseases. Am J Med Genet Part A. 2019;1–8. https://doi.org/10.1002/ajmg.a.61124
3. Chung CCY, Hong Kong Genome Project, Chu ATW and Chung BHY (2022) Rare disease emerging as a global public health priority. Front. Public Health 10:1028545. doi: 10.3389/fpubh.2022.1028545
4. National Policy for Rare Diseases 2021, Ministry of Health and Family Welfare, Government of India, URL available from https://rarediseases.mohfw.gov.in/uploads/Content/1624967837_Final-NPRD-2021.pdf retrieved on 06.09.2023, 12.00 IST.
5. "Orphan Drug Act of 1983" (PDF). US Food and Drug Administration. 4 January 1983. Retrieved 27 October 2015.
6. Kumar H, Sarma P, Medhi B. Orphan drugs: Indian perspective. Indian J Pharmacol. 2017 Jul-Aug;49(4):267-269.
7. Kumar S. Orphan drugs and disease : Regulatory and Legal framework [Internet]. Lexology. TMT Law Practice; 2022 [cited 2023 Oct 3]. Available from: https:// www.lexology.com/ library/detail.aspx?g=8c24664d-4f3f-47a1-8c86-41a972b772fb
8. Baynam, G.S., Groft, S., van der Westhuizen, F.H. et al. A call for global action for rare diseases in Africa. Nat Genet 52, 21–26 (2020). https://doi.org/10.1038/s41588-019-0552-2
9. Luzzatto L, Makani J. Treating rare diseases in Africa: the drugs exist but the need is unmet. Frontiers in Pharmacology. 2022 Jan 10;12:770640.
10. Who we are [Internet]. Irdirc.org. [cited 2023 Oct 3]. Available from: https://irdirc.org/who-we-are-2/
11. List of rare diseases [Internet]. National Organization for Rare Disorders. [cited 2023 Oct 3]. Available from: https://rarediseases.org/rare-diseases/
12. Yang, G., Cintina, I., Pariser, A. et al. The national economic burden of rare disease in the United States in 2019. Orphanet J Rare Dis 17, 163 (2022). https://doi.org/10.1186/s13023-022-02299-5
13. 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.
14. Khosla N, Valdez R. A compilation of national plans, policies and government actions for rare diseases in 23 countries. Intractable & Rare Diseases Research. 2018 Nov 30;7(4):213-22.
15. Montserrat A, Taruscio D. Policies and actions to tackle rare diseases at European level. Annali dell'Istituto Superiore di Sanità. 2019 Sep 23;55(3):296-304.
16. Boycott KM, Lau LP, Cutillo CM, Austin CP. International collaborative actions and transparency to understand, diagnose, and develop therapies for rare diseases. EMBO Molecular Medicine. 2019 May;11(5):e10486.
17. Chung CC, Hong Kong Genome Project, Chu AT, Chung BH. Rare disease emerging as a global public health priority. Frontiers in public health. 2022 Oct 18;10:1028545.
18. Taruscio D, Salvatore M, Lumaka A, Carta C, Cellai LL, Ferrari G, Sciascia S, Groft S, Alanay Y, Azam M, Baynam G. Undiagnosed diseases: Needs and opportunities in 20 countries participating in the Undiagnosed Diseases Network International. Frontiers in Public Health. 2023 Mar 2;11:1079601.
19. Shafie AA, Chaiyakunapruk N, Supian A, Lim J, Zafra M, Hassali MA. State of rare disease management in Southeast Asia. Orphanet journal of rare diseases. 2016 Dec;11(1):1-1.



**Scientific Editor:** Dr. Deepa Bhat (JSS AHER) **Editorial Adviser:** Prof. Basavanagowdappa Hathur (JSS AHER) & Mr. Madhusudan Bandyopadhyay (NAM S&T Centre) ✸ **Staff Editor:** Ms. Jasmeet Kaur Baweja ✸ **Compilation & Design:** Mr. Pankaj Buttan
**Published by:** Dr. Amitava Bandopadhyay, Director General, Centre for Science & Technology of the Non-Aligned and Other Developing Countries (NAM S&T Centre), Core 6A, 2nd Floor, India Habitat Centre, Lodhi Road, New Delhi-110003 (India)
**Phone:** +91-11-24645134, 24644974 **Email:** namstcentre@gmail.com **Website:** https://namstct.org