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A Review on Rare Disease

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Abstract: Disease heterogeneity and geographic distribution have become issues for treatment and research options for rare diseases. Limited access to basic care, delays in diagnosis, and limited or no treatment options increase the burden on patients. Driven by these challenges, patient organizations and the government of India are playing an important role in meeting the needs of patients and improving their physical and mental health. This article aims to describe India's progress in rare diseases through a brief review of its knowledge and research on 450 and more diseases and its involvement in government projects.

Keyword
Rare disease, NGO's, Foundations, Awareness, Treatment, Society etc.

Introduction

It is a disease that affects a small group of people, has a very low incidence, and is rare compared to other diseases in society. The World Health Organization defines a rare disease as a lifelong disease or condition with a prevalence of 1 or less per 1,000 living people. Although foreign countries have their own image definitions, their specific laws concern details of population, treatment and assets. In other cases rare diseases have no international recognition. In the United States, the Orphan Drug Act designates rare diseases that affect fewer than 200,000 people in the United States [(1)].

Europe defines rare diseases as life-threatening or serious diseases that affect no more than 5 in 10,000 people. Japan defines rare diseases as diseases with fewer than 50,000 cases. There are approximately 6000 to 8000 rare diseases worldwide, and new rare diseases are being reported. Like other developed countries, India currently does not have a standard definition of rare diseases and lacks epidemiological data. According to statistics, the population of rare diseases and disorders in India is 72,611,605 as per the ongoing national census data published in 2011[(2)].

Indian Perspective

In India, 1 in 10,000 diseases are considered rare [(3)].450 rare diseases have been recorded in India so far [(4)].The number of patients suffering from rare diseases in India is still unknown. Although there is a lack of data to assess the burden, morbidity and mortality of rare diseases. Less common diseases are hemophilia, thalassemia, sickle cell anemia and primary anemia, autoimmune disease and lysosome storage disease [(3)].

An initiative of the Government of India, Central Drugs The Standard Control Organization (CDSCO) has issued a clinical trial waiver notice for approval of a new drug in the Indian population, for drugs that are already approved outside India, and that was stated that this waiver may only be possible in the case of orphan drugs and medicines indicated for diseases and conditions where there is no therapy[(5)].The Indian Council of Medical Research [ICMR] published the India List of Rare Diseases in 2017. The list will facilitate access to treatment by making it easier to identify patients with pain. This list also helps you understand the spread and effects of the

disease. The Government of India under the Ministry of Health and Family Welfare has started focusing on rare diseases and recently the Ministry of Health and Family Welfare has formulated the country's first policy on rare diseases. Table 1 lists various efforts by Indian rare disease organizations to support patients. There are disease-specific organizations and they provide necessary information for patients with rare diseases. Table 2 provides a list of disease-specific organizations operating in India only.

Table 1: List of rare disease organizations in India

S. No.	Name Of Organization	Website
1.	Metabolic errors and Rare Disease Organization of India - MERD	http://merdindia.com/index.html
2.	Organization for rare diseases India - ORDI	http://www.i-ord.org/
3.	National Organization for Rare disorders - NORD	https://rarediseases.org/
4.	Guardian	http://guardian.meragenome.com/home
5.	Foundation for Research on Rare Diseases and Disorders	https://rarediseases.org/organizations/foundation-for-research-on-rare-diseases-and-disorders/

1. Metabolic Errors and Rare Disease Organization of India - MERD

MERD India Foundation works to create awareness about metabolic and rare genetic diseases. The organization provides physical and emotional support to parents of affected children and conducts regular child screening across India.

2. Organization for Rare Diseases India - ORDI

ORDI [Rare Disease Organization of India] is a national NGO that provides a platform to highlight the negative impact of rare diseases on patients in India. The organization is committed to providing early diagnosis and early treatment to patients with rare diseases every year. ORDI collaborates with the public and private sectors to carry out mandatory testing of infants and support the research and development of orphan drugs.

3. National Organization for Rare Disorders - NORD

NORD is a non-profit organization operating in India and the United States. NORD often advocates for the concerns of individual patients and minority patient groups. NORD is dedicated to advancing innovative treatment, diagnosis and treatment of rare diseases through knowledge, research and patient services. They support research that benefits patients with rare diseases. NORD's research services help researchers develop effective diagnostic tools as well as treatment plans.

4. Guardian

Observer is a collaboration between CSIR and the Institute for Genomics and Integrative Biology (IGIB). Doctors and research laboratories are working together to understand the genetic and molecular mechanisms underlying rare genetic diseases. The group also works to support research and development of orphan drugs.

5. Foundation for Research on Rare Diseases and Disorders

Rare Diseases and Cancer Research is a non-profit, non-governmental organization. Rare Diseases India provides research information on rare diseases. It involves studying rare diseases, collecting information on classification of rare patients, donating rare biological organisms (blood, tissue, etc.), and promoting awareness for fewer patients. The Foundation provides a platform for countries in South Asia by creating a rare disease information database with country-specific information and identifying rare disease names and conditions.

Table 2: List of disease specific organizations

S. No.	Name Of Organizations
1.	Indian Rett Syndrome Foundation
2.	Hemophilia Federation of India
3.	DART[Dystrophy Annihilation Research Trust]
4.	Indian Society for Primary Immune Deficiency
5.	Fragile X Society India
6.	Lysosomal Storage Disorder Support Society
7.	Thalassemia and Sickle Cell Society [TSCS]
8.	Society for Hemophilia Care, India
9.	Sjorgen's India
10.	World Without GNE Myopathy [WWGM]

1. Indian Rett Syndrome Foundation

Rett Syndrome Association of India is a national association of parents, doctors, researchers, medical professionals and caregivers of children with Rett syndrome. Reports show that 1 in every 10,000 to 15,000 women born in the world is Rett. The foundation was established on January 27, 2010. IRSF's mission is to understand people living with Rett Syndrome in India. They run counseling services and spread awareness about managing Rett syndrome.

2. Hemophilia Federation of India - HFI

Hemophilia Institute of India [HFI] is the only organization in India working for the benefit of hemophilia [PwH] patients. The organization's mission is to provide quality care, education, psychological support, and financial recovery to reach PwH and help them live trouble-free lives. HFI maintains a database of hemophilia clinics across India and distributes them to various cities in collaboration with the Ministry of Health and Family Welfare.

3. Dystrophy Annihilation Research Trust-DART

DART [Malnutrition Eradication Research Foundation] is India's first research center to find a treatment that can help reduce and reverse Duchenne Muscular Dystrophy at the genetic level,improving its effects on children's quality of life.

4. Indian Society for Primary Immune Deficiency- ISPID

The organization's mission is to provide support to patients with pelvic inflammatory disease and to help their families achieve the best possible physical, mental, emotional and social health. ISPID encourages collaboration in the treatment of partners and establishes policies regarding the needs and decisions of research and studies on the important area of immune system pain.

5. Fragile-X Society India

Awareness of public administration and Fragile X Syndrome. The Foundation is dedicated to educating families with affected children on a broader understanding of the impact of Fragile X Syndrome and building a global network of people working on Fragile X Syndrome research.

6. Lysosomal Storage Disorder Support Society - LSDSS

The Lysosomal Storage Disease Support Foundation is a non-profit organization dedicated to raising public awareness and education about the effects of LSD. The organization documents and leverages international research on the causes, treatment and management of these diseases. LSDSS is actively working to improve existing guidance and resources for the diagnosis, counseling, and treatment of lysosomal storage diseases.

7. Thalassemia and Sickle Cell Society- TSCS

The Thalassemia and Sickle Cell Foundation is dedicated to helping people with thalassemia, with the goal of curing and extending the lives of every child with thalassemia. The institution's laboratories are well equipped with advanced laboratory and treatment facilities and provide free services to thalassemia patients. The organization also provides medicines at affordable prices, records the normal development of children, and provides free medical care and genetic testing.

8. Society for Hemophilia Care, India- SHC

SHC is a national initiative focused on the treatment of patients with hemophilia and other bleeding disorders. SHC works with individuals, governments and businesses to promote safe, effective, affordable and effective treatment for patients with hemophilia and other bleeding disorders. The organization also organizes awareness and education programs on the effects and prevention of hemophilia.

9. Sjorgen's India

Sjorgen India is a voluntary foundation that supports patients by creating awareness about Sjögren's disease. The organization is known to provide a platform where people suffering from Sjögren's syndrome can interact with doctors and researchers across the country.

10. World without GNE Myopathy – WWGM

World without GNE Myopathy [WWGM] is an organization dedicated to the treatment of GNE myopathy and other rare diseases. As we all know, the Foundation's mission is to raise awareness of rare genetic diseases among patients and the international community and to provide information and support to people affected. WWGM's primary mission is to promote research and demonstrate treatments for GNE myopathy and other rare genetic diseases.

Challenges

Rare diseases are particularly challenging for scientists for many reasons, including the worldwide spread of the disease, the high incidence and rarity of all diseases, and the limited availability of accessible data. They are also very burdensome and expensive for patients, their families, contacts and relationships [(6)]. Hemophilia, thalassemia, sickle cell anemia and primary wasting, autoimmune diseases, lysosomal storage diseases such as Pompe disease, Hirschsprung disease, Gaucher disease, cystic fibrosis, chlorosis, hemangiomas and some muscular dystrophies are generally well-known diseases. Rarely recorded. There is a lack of knowledge among patients and caregivers in the medical community and a lack of health insurance policies, plans, and clinics. But the bigger problem is the lack of discussion about the disease and knowledge. Lack of transportation and expensive medical care will continue to be the biggest problems. Rights of the Mentally Disabled Person do not cover rare diseases. There is no law that recognizes disability treatment and denies patients opportunities and benefits. Support for the patient's family is limited. Currently, only some international pharmaceutical organizations collect drugs for the treatment of rare diseases.

There is an urgent need for a multinational public health program in India to screen newborns for genetic diseases. Until now, nationwide data was not available due to lack of communication. In recent years, a non-governmental

organization has started to register births. Genetics laboratories should have an independent scientific assessment, as most laboratories now follow international guidelines or necessary changes in individual regulatory actions, good job Considering the Indian context, personal exome sequencing for rare diseases is challenging mainly due to cost issues. Insufficient bioinformatics facilities will reduce diagnostic accuracy. The complexity of rare diseases is further compounded by the ethnic diversity of India's population. Approximately 95% of rare diseases receive no treatment, and less than 1 in 10 patients receive specialized treatment.

The main problem is the availability of the drug, which is solved by self-medication. Where drugs are available, they are sold at high prices, causing a significant impact on the resources of families, healthcare systems, and donors [7–10]. Rare disease information in India. It is important to assist the patient with medical decisions and encourage them to get the right treatment, and early conclusions are also important, but diagnosis is often delayed because awareness among patients and doctors is low. It takes seven years from the onset of symptoms of a rare disease to its end. During this period, patients experience many symptoms, health problems, stress, try many tests, and apply to many specialists and hospitals [11,12].

This diagnostic process is tedious, requires advanced technology and is therefore very expensive. Many parents face autism without realizing the condition. The Indian subcontinent is one of the most diverse regions in the world, with a population of approximately 1.5 billion, including approximately 5,000 different ethnic groups. Geographical, semantic or social boundaries, such as restricting marriage between groups, ensure that a significant proportion of spouses are of the same lineage. This may promote the transmission and proliferation of some rare diseases [13]. Due to the rarity of these diseases, pharmaceutical companies have determined that drug development and improvement do not benefit them [14]. Patients are dispersed over a wide area, making distribution of medications difficult. The lack of current or up-to-date information on patient conditions prevents companies from developing effective drugs.

Conclusion & Future Perspective

Although 450 rare diseases are known to exist in the Indian population, comprehensive information on the major diseases is not available. The Institute of Rare Diseases and Research provides statistics on the number of people living with rare diseases in Indian states; this rate is above the global average. In developing countries such as India, there is no epidemiological study even on the classification of rare diseases. Lack of information at the internal level often leads to late diagnosis or misdiagnosis. Recently, the Indian government has become more aware of the importance of public policies, especially for the treatment of rare diseases. The lack of legislation providing incentives for pharmaceutical organizations to innovate continues to lead to a lack of care for orphan drugs and diagnostics. This situation increases the financial burden required for the patient to go through the diagnosis and treatment process [10].

Genetic diseases are likely to proliferate in India, as genetic diseases occur through mutations in the population and affect reproduction in families known to be at risk of genetic diseases. Genetic counseling is an important aspect of the prevention and control of genetic diseases, targeting families born affected or families with a family history of the disease. Due to the competitive nature of rare disease research, genetic diseases are difficult to approach through healthcare/epidemiology and prevention studies, for example, providing genetic counseling through healthcare [9]. In recent years, rare microdeletion/duplication syndromes have been recognized along with the chromosomal microarray level. Due to lack of cost, many centers use multiplex ligation-dependent probe amplification assays for the diagnosis of subtelomeric and common microdeletion/duplication syndromes [8].

India's ongoing research and treatment programs hold promise for reducing misdiagnoses of rare diseases. Advances in DNA sequencing and reductions in costs have made it possible to diagnose rare genetic diseases [3].Improving capacity in rare disease research will have a major impact on public health [15]. It is important to create a database for predicting influencers. The government should initiate programs for the diagnosis, treatment and promotion of rare diseases.

Improving rare diagnosis and treatment in three key areas: high genome integration, prenatal diagnosis and prevention, treatment, and advances in gene therapy [16]. Orphan drug trials require greater attention and the development of new trial models that recognize the small number of patients affected by these diseases. Even among doctors, knowledge about the disease is limited; therefore, collaboration between rare patient organizations, researchers, and regulatory agencies can help create new treatments for rare diseases.

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