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India Rare Disease Initiatives – A Review

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ABSTRACT

Disease heterogeneity and geographic dispersion has becomes an obstacle among rare disease treatment & research options. Finite access to convenient care, delayed diagnosis and limited or non-existing treatment options over burdens the patients. Motivated by these challenges, the patient organizations and Indian government has played a critical role in upholding patient needs and aid their physical and mental strength. This article intends to shed light by making a short review regarding the progress in rare disease initiatives, awareness and research activity developments in India in tackling 450 and more such diseases and their contributions in par with government activities.

Keywords: Rare disease, NGO's, Foundations, Awareness, Treatment, Society

INTRODUCTION

Health circumstance of especially low incidence that impacts a small range of population as compared with other commonly diseases among the population are attributed as Rare Diseases. World Health Organization defines rare diseases as lifelong disease or disorder condition with a prevalence of 1 or less, per 1000 population. Even though different nations have their own interpretation to in shape their specific requirements with background of their population, health care system and asset. In other words there is no universally recognized definition for rare diseases. In United States, Orphan Drug Act which defined rare diseases as those affecting fewer than 200,000 people in the US [1]. Europe defines rare diseases as a life-threatening or chronically debilitating condition affecting no more than 5 in 10,000 people. Japan identifies rare diseases as diseases with fewer than 50,000 prevalent cases. Globally around 6000 to 8000 rare diseases exist with new rare diseases being reported. Like any other developing countries, currently India has no standard definition for rare diseases and since there is no epidemiological data. It is statistically estimated that, in India, the rare disease and disorder population were 72,611,605 as per published data of national population census of 2011 or later [2].

Indian Perspective

In India for a disease to be defined as rare is 1 in 10,000 [3]. In India, so far 450 rare diseases are recorded [4]. There is no clear idea about the number of patients afflicted with different rare diseases in India. Even though no figures on burden, morbidity and mortality rates associated with rare diseases are analyzed. The most common rare diseases reported are hemophilia, thalassemia, sickle cell anemia and primary immunodeficiency, auto-

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immune diseases, lysosomal storage disorders [3].The Indian government initiative, the Central Drugs Standard Control Organization (CDSCO) issued a notice regarding remission of clinical trial for approval of new drug in the Indian population, for drugs which are already approved outside India, and it was mentioned that this waiver can only be possible in case of orphan drugs for rare disease and drugs indicated for diseases and condition where there is no therapy [5]. Indian Council of Medical Research [ICMR] launched Indian rare disease registry in 2017.The registry favors the identification of patients which will help the access to the treatment. The registry also beneficial for understanding the spread of the disease and the consequences. Under the ministry of Health and Family Welfare Government of India have initiated anappreciable work on rare diseases along with a recent Union ministry of health and family welfare ministry draft of the country's first national policy pertaining to rare diseases. Table 1 shows the list of Indian rare disease organizations put their efforts to provide support the patients in all aspects. Some organizations are disease specific and they contribute necessary awareness to the patients suffering particular rare diseases. Table 2 specifies the list of disease specific organizations actively working only in India.

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	Guardian	http://guardian.meragenome.com/home
4	National Organization for Rare disorders - NORD	https://rarediseases.org/
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 is working towards the awareness about inborn metabolic errors and rare genetic disorders. The organization provides physical and emotional support to the parents of affected children and conduct effective programs on newborn screening in India at a regular basis.

2. Organization for Rare Diseases India - ORDI

ORDI [Organization for rare diseases India] is a national level NGO organization serving the platform for emphasizing the adverse effects of the patients with rare diseases in India. The organization is always engaged in early diagnosis and to provide early treatment options for rare disease patients throughout the year round. ORDI collaborate with public-private sectors for mandatory new born screening and in promoting research& Orphan drug development.

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3. Guardian

Guardian is a collaboration of CSIR and Institute of Genomics & Integrative Biology [IGIB]. Clinicians and research labs are in collectively working towards understanding the genetic and molecular basis behind the rare genetic disorders. The group also serves in the promotion of orphan drug research and manufacture.

4. National Organization for Rare Disorders - NORD

NORD is not-for-profit organization working in India as well as in USA.NORD actively speaks for the concerns of individual patients, patient support groups for rare disease. NORD is dedicated for the development of treatment strategy, diagnosis, and cure of rare disorders through awareness, research, and patient services. They encourage researches for the welfare of rare disease patients. Research Grant Program of NORD is beneficial for scientists for the development of efficient diagnostic tools as well as treatment plans.

5. Foundation for Research on Rare Diseases and Disorders

Foundation for Research on Rare Diseases and Disorders is a not-for-profit non-governmental organization. Rare disease India provides scientific data resource dedicated to rare diseases. It involves review articles on rare diseases, rare disease patient distribution data collection, donating rare disease bio-specimen [blood, tissues etc.] and providing awareness for rare disease patients. The foundation provides a platform for the entire south Asian countries by developing rare diseases information database with country specific data and identify existing scattered rare diseases and disorders registries.

Table 2: List of disease specific organizations

S. No.	Name of Organization	Website
1	**Indian Rett Syndrome Foundation**	**http://www.rettsyndrome.in/**
2	**Indian Society for Primary Immune Deficiency**	**http://ispid.org.in/**
3	**Society for Hemophilia Care, India**	**http://www.shcindia.org/**
4	**Lysosomal Storage Disorder Support Society**	**http://www.lsdss.org/whoweare.html**
5	**Hemophilia Federation of India**	**http://hemophilia.in/**
6	**Fragile X Society India**	**http://www.fragilex.in/about-fragile-x.html**
7	**Sjorgen's India**	**http://www.sjogrensindia.org/**
8	**DART[Dystrophy Annihilation Research Trust]**	**https://dartindia.in/**
9	**World Without GNE Myopathy [WWGM]**	**http://gne-myopathy.org/**
10	**Thalassemia and Sickle Cell Society [TSCS]**	**https://www.tscsindia.org/**

1. Indian Rett Syndrome Foundation

Indian Rett Syndrome Foundation is a national wide collaboration of Parents, Doctors, Scientists, Health professionals and care takers of children with Retts syndrome. Reports reveal worldwide in 1 of every 10,000 to 15,000 female births are Rett patients. The foundation established on 27th January, 2010. The undertaking of IRSF is to perceive humans with Rett syndrome in India. They conduct counseling programs and spread awareness on the management of Rett syndrome.

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2. Indian Society for Primary Immune Deficiency- ISPID

The goals of the Society are to serve as advocates for sufferers with PID and assist their families on the subject to attain the most reliable physical, mental, psychological and social health. ISPID promote clinical collaboration amongst contributors and make policies concerning requirements & entertain research and studies in primary immune deficiency disorders in any of its factors.

3. Society for Hemophilia Care, India- SHC

SHC is a national wide initiative extensively dedicated for people suffering from hemophilia and other genetic bleeding disorders. SHC jointly works together with individuals, government & industry for facilitating safe, quality, affordable & ethical treatment for hemophiliac patients and other bleeding disorders. The society also organizes awareness programs and education about impact and prevention of Hemophilia.

4. Lysosomal Storage Disorder Support Society - LSDSS

Lysosomal Storage Disorder Support Society is a non-profit organization working towards to reinforcing awareness and educates the society about the effects of LSD's. The Society records and utilizes the worldwide research into the causes, treatment and management of these diseases. LSDSS is actively engaged in works to increase the guidance and facilities available for diagnosis, counseling and treatment of lysosomal storage diseases.

5. Hemophilia Federation o f India - HFI

Hemophilia Federation India [HFI] is the India's only umbrella organization operating for the interest of the persons with hemophilia [PwH]. The federation is working with a goal to reach out to PwH and offer overall excellent care, education, low cost treatment psycho-social assist, and economic rehabilitation and therefore assist them to lead a life without impairment . HFI maintain a database of hemophilia treatment centers across India and works distributed by regionally and jointly works with Ministry of Health and Family Welfare.

6. Fragile-X Society India

The Society upholds public and professional awareness concentrated on Fragile X syndrome. The foundation works in guiding the families with affected children with a broad understanding of the impact of Fragile-X syndrome and creates a worldwide network among the people who are working on Fragile-X syndrome research.

7. Sjorgen's India

Sjorgen's India is a volunteer-led foundation which focuses on patient empowerment by the way of creating attention on Sjogren syndrome. The organization is known to provide a platform for the people who are suffering from Sjogren syndrome to have interaction with doctors and scientist across the country.

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8. Dystrophy Annihilation Research Trust-DART

DART [Dystrophy Annihilation Research Trust] is the first research lab in India aimed towards finding a treatment option to help alleviate and reverse Duchene Muscular Dystrophy at the genetic level, enhancing the quality of life of affected children.

9. World Without GNE Myopathy – WWGM

World Without GNE Myopathy [WWGM] is an organization which was founded in concern with the therapies for GNE Myopathy and other rare diseases. The foundation is known to work on a mission to generate awareness about this rare genetic disorder amongst patients and communities worldwide and provide information and support to the ones affected. The major objective of WWGM is to promote research that will accelerate discovering cures for GNE Myopathy and other rare genetic disorders.

10. Thalassemia and Sickle Cell Society- TSCS

Thalassemia and sickle cell society committed to help the thalassemia patients with an objective is to treat all thalassemia children and adds their life expectancy. The society laboratory is well equipped with the advanced diagnostic and treatment facility to thalassemia patients free of cost. Society also provides medicines at subsidized rates, and record regular growth of children, free medical and genetic counseling.

Challenges

Rare diseases present unique challenges to researchers due to several reasons such as the worldwide conveyance of patients, multifaceted nature and low pervasiveness of every disease, and constrained accessibility of data. They are additionally overpowering and expensive for patients, their families, networks, and society [6]. Hemophilia, thalassemia, sickle cell anemia and primary immunodeficiency, auto-immune diseases, lysosomal storage diseases for example-pompe disease, hirschsprung's disease, gaucher's disease, cystic fibrosis, haemangioma and certain types of muscular dystrophy are the most well-known rare diseases recorded. Patients and caretakers struggles with in adequate awareness among the medical fraternity and an absence of devoted social insurance policies, plans and diagnosis facilities. However more severe challenge is the lack of counseling and database of rare diseases. The inaccessibility and expensive treatment stay perhaps the great hurdles. Rare diseases are not included under the Rights of Persons with Disabilities Act. No law recognizes medical disability, denial of facilities and benefits for patients. The supportive cares for the patient families are prohibited. At present, limited worldwide pharmaceutical organizations are assembling drugs for rare diseases.

In India, requirement for more national public health programs for newborn screening are in dire need for genetic disorders. So far nationwide data has not been possible due to inadequate inter institutional communication. A registry for birth defect has additionally been started over recent years by a nongovernment association. An independent research facility measures are required for genetic diagnostic labs as presently most laboratories are following international guidelines or appropriate modifications by individual quality control norms. Considering Indian scenario personalized exome sequencing of rare disease practically difficult mainly the cost is concerned. Lacking well established bioinformatics facilities downs the accuracy of diagnosis. The ethnic diversity of Indian population intensifies complexity of rare disease. Approximately 95 per cent of rare diseases have no accepted treatment and less than one out of 10 patients get specific treatment. The major issue is accessibility of

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medications, which the administration approach itself underscored. Where medications are accessible, they are high costly, putting immense strain on resources of families, health systems and donor agencies [7-10]. There is limited awareness of rare diseases in India. Patient help and support gathering right from clinical determination, direction for treatment is the critical early conclusion is pivotal yet because of lack of awareness patients and a few doctors diagnosis of often delayed. It takes seven years to conclude a disease as rare after the beginning of symptoms. During this time, patients experience a variety of symptoms, health issues, nervousness, attempting a variety of laboratory tests and visiting various specialists and hospitals [11,12]. This diagnostic procedure is tedious and requires a high-end technology, making it costly. Parents experience plenty of mental traumas without realizing the condition. The Indian subcontinent is one of the most hereditarily assorted places on Earth, with a populace moving toward 1.5 billion that incorporates about 5,000 well-characterized subgroups. Geographic, semantic or social boundaries, for example, confinements on marriage between groups, improve the probability that mates share a significant part of the equivalent ancestry. This can prompt the propagation and multiplication of certain rare, recessive diseases [13]. Because of the uncommon occurrence of these diseases drug makers discover advancement and improvement of medications for them unfruitful [14]. The widespread of patients make difficult for the distribution of medications. The lack of a database for the condition or updates of patient's current state discourage companies to produce efficient drugs.

CONCLUSION & FUTURE PERSPECTIVES

Though 450 rare diseases are known to exist in the Indian population, the quantitative information concerning disease predominance does not exist. The statistical data of the number of individuals experiencing rare diseases in Indian states, are higher from worldwide predominance rates, have been given by the Foundation for Research on Rare Diseases and Disorders. The absence of prevalence studies has even prompted the misled classification of diseases as rare conditions, in developing countries like India. The inadequate awareness at the intrinsic level, which frequently brings about in late diagnosis or misdiagnosis. Recently the Government of India has come to understand the significance of dedicated public policy regarding the treatment of rare diseases. The absence of enactment giving innovative work motivating forces to pharmaceutical organizations keeps on energizing the carelessness of orphan drug and diagnostic methods. This further represents a high economic burden on the patience to access the diagnostic and treatment procedures [10].

As genetic disorder emerges in the population through spontaneous mutations and affected births in families with a known risk of a genetic disorder, in absolute numbers, the birth commonness of genetic disorder is probably going to be high in India. Genetic counseling is the primary apparatus for the prevention and control of genetic disorders, directed at families with an affected birth or with a family ancestry of the disorder. Because of the methodological challenges of studying rare disorders, it is hard to approach genetic disorder from a general wellbeing/epidemiology perspective and investigate prevention that is delivery of genetic counseling from a health systems standpoint [9]. In recent years, with the accessibility of chromosomal microarray stages, rarer micro deletion/duplication syndromes are additionally being recognized. Due to cost restrictions, numerous centers utilize multiplex ligation-dependent probe amplification assay for diagnosis of subtelomeric and common micro deletion/duplication syndromes [8]. Innovative diagnostic and therapeutic ongoing programs in India are a promising sign in drastically decrease false positive diagnosis of rare disease. The advancements and dynamic reduction in cost of DNA sequencing makes possible to diagnose rare genetic diseases [3]. Improving the ability to conduct research on rare diseases would have a significant impact on population health [15]. Developing a database is essential to estimate the population affected. Government has to initiate scheme for rare disease diagnosis, treatment and support. Upgrade rare disease diagnosis,

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research and treatment in three main areas: high throughput genomic sequencing, prenatal diagnosis and disease predisposition, and advancements in targeted therapies and gene therapy [16]. Orphan drug clinical trials should need more attention and need to develop innovative trial designs that recognize the small patient populations which these conditions affect. Expertise in rare diseases is limited, even among healthcare professionals and hence a collective effort of rare disease patient organization, researchers, and regulatory authorities could help to develop new treatment options for rare disease.

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