Short Communication

Rare diseases are not actually rare in India

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Abstract
Rare diseases, also known as orphan diseases, pose significant clinical and economic burdens, affecting millions of people worldwide. With over 7,000 known rare diseases globally, 80% of which have genetic origins, the symptoms vary not only from disease to disease but also from patient to patient, even among those suffering from the same disease. Most of these diseases are degenerative and progressive in nature. In India, over 70 million people are affected by rare diseases. Delays in early diagnosis due to lack of relevant genomic information and scientific knowledge, as well as insufficient healthcare infrastructure and difficulties in accessing treatment are some of the common challenges faced in the treatment of rare diseases. This study provides an overview of global and national efforts to address rare diseases, the barriers to diagnosis and treatment and the need for coordinated research, policy, and healthcare solutions.

Keywords: Orphan disease, NCATS, RARE List™, ICMR, IGIB

Introduction

Rare diseases pose clinical and economic burden as well as a significant challenge for health systems. About 6,000 to 7,000 patients are reported to be suffering from rare diseases, for most of which no specific treatment options are available. A disease or disorder is defined as rare in Europe when it affects less than 1 in 2000 in the population and in the USA, it is set to be at 1 / 200,000 at any given time. A rare disease is often referred to as an orphan disease. They are characterized by a broad diversity of disorders and symptoms that vary not only from disease to disease but also from patient-to-patient suffering from the same disease. 80% of the rare diseases have genetic origins and others are the result of infections, allergies, and environmental causes. Most of them are degenerative and proliferate in nature and 50% of rare diseases affect children. Most common symptoms can hide underlying rare diseases, leading to misdiagnosis. In most of the cases, there may not be effective cure and can cause high level of pain and suffering to the patients as well as their families.

Early diagnosis is a major challenge in rare diseases and most cases remain undiagnosed for a long period of time. Majority of the cases take more than 7 years to diagnose. During this period the patients experience poor physical and mental health problems. They also try a variety of laboratory tests and often visit super-specialty doctors and hospitals. It is very important to put an end to this diagnostic dilemma. Once the patient receives a proper diagnosis, they can move to next steps of disease management looking for different treatment options, lifestyle changes etc. More than 7000 rare diseases are identified globally and about 450 of them have been reported in India. For most diseases treatment is unavailable even after proper diagnosis, because only about 5 percent of rare diseases have a treatment approved by the Food and Drug Administration. Most of them are very expensive and unaffordable to common man. Insurance policies most of the time do not cover these ongoing (lifelong) treatment expenses.

Common Problems faced and international initiative

The major delay in rare disease diagnosis is due to the lack of quality of genomic information and scientific knowledge. The lack of appropriate quality healthcare engenders inequalities and difficulties in access to treatment and care. Most of

the time, this situation leads to heavy social and financial burdens on patients and family. The initial misdiagnosis is common in most cases of rare diseases because of the board diversity and relatively common symptoms associated with other diseases. Due to the spatiality and verity of rare diseases, research needs to be global to ensure that policy-making experts, healthcare providers, basic researchers, and clinicians are connected. In addition to that clinical trials are multinational and that patients can benefit from the pooling of data and resources across borders. Initiatives such as the European Reference Networks, the International Rare Disease Research Consortium and the EU Framework Programme for Research and Innovation Horizon 2020 support international level collaborative research on rare diseases.

The incidence of rare diseases globally and specific to India

The major concern in rare diseases is that it cannot be determined by a universal definition. However, the importance of having a consistent definition is well acknowledged. Adopting a standard definition of rare disease is a pre-requisite for public policy development. There are approximately 350 million patients affected by about 7000 known rare diseases. Rough estimates indicate that over 70 million people in India are affected by rare diseases, many of whom may still not have a diagnosis. Different rare diseases database including Orphanet database is updated every year to accommodate new diseases that are being reported. Orphanet database is maintained by the European Union. We do not yet have accurate statistics on the incidence or prevalence of rare diseases in India. This is mainly because of the lack of definition and more importantly, due to the lack of diagnostic tools and equipment and systematic data collection systems in India. Half of the rare diseases are early onset childhood diseases. About 80% of all rare diseases are genetic in origin, most of them monogenic. The US National Institutes of Health initiatives such as the Undiagnosed Diseases Network (UDN) and the international rare diseases research consortium (IRDiRC) aim to address this challenge by accelerating the speed of diagnosis. The goal is to bring the average time to diagnosis down to one year.

Time to time, scientific and patient communities have expressed the need for government initiatives towards rare diseases. The first attempt to bring together all experts of rare diseases under a common platform was initiated by Indian National Science Academy (INSA), which conducted the first of the kind rare disease workshop entitled "To Develop a Scientific Program for Research on Rare Diseases" in 2016, which deliberated on issues such as definition of "Rare disease," rare disease awareness, rare disease research avenues, policy framework for boosting and incentivizing research and development efforts and framing suitable legislation to ensure involvement of the State in fulfilling the special needs of rare diseases. In the INSA rare disease workshop (2016), the honourable Drug Controller General of India stated that a policy for accelerated clearance of orphan drugs and fast-track approval is not in place because government needs clear-cut recommendations regarding the definition of rare disease, mechanism for fast-track approval (e.g., waiver of a specific phase in orphan drug clinical trial). He again stated that genetic differences in Indian population warrant studies from India, rather than using data from studies in other countries. He also invited for expert suggestions on the need of changes in the drugs and cosmetic act to meet the requirements of research in rare disease.[1]

The Genetic and Rare Diseases Information Center (GARD) is a program of the National Center for Advancing Translational Sciences (NCATS) and is funded by two associate institutions of the National Institutes of Health (NIH): NCATS and the National Human Genome Research Institute (NHGRI). GARD provides the public with access to current, reliable, and easy-to-understand information about rare or genetic diseases in English or Spanish. NORD's database provides brief introductions for patients and their families about more than 1,200 rare diseases. This is not a comprehensive database considering the fact that there are nearly 7,000 diseases considered rare in the U.S.

RARE List™

The RARE List™ comprises approximately 7,000 different rare diseases and disorders affecting more than 300 million people worldwide. Some common diseases are included on the RARE List™ because in the United States one of the primary criteria for recognizing a disease as rare is the prevalence of the disease fewer than 200,000 cases. Diseases such as malaria are quite common in some parts of

the world but are considered rare in the United States. Other diseases such as Cancer or Alzheimer's are not rare diseases, but certain forms of these diseases are considered rare.[2]

The Indian Council of Medical Research (ICMR) initiative

ICMR has been providing financial assistance to projects for orphan disease research and for sponsoring/organizing workshops /conferences /training programs on rare diseases. It has also taken the initiative in the preparation of a registry for rare disease. [3,4] This is referred to as National Initiative for Rare Diseases (NIRD), organized jointly by ICMR, AIIMS, JNU, and PRESIDE. The first step in this endeavour is to identify patients with the rare disease. "Indian rare disease registry" was launched on April 27, 2017. This registry is intended to cover all rare and ultra-rare diseases prevalent in India. The registry was first intended to be hospital-based and later population based. The objectives of the registry include: to identify patients having rare diseases, to use that data for policy framing and to guide future research. The registry may also enable proper and easy monitoring of the diseases including their prevalence, incidence and natural history with regard to the Indian context.

Council of Scientific & Industrial Research (CSIR) and Institute of Genomics & Integrative Biology (IGIB) initiative

IGIB, New Delhi, has conducted a project funded by CSIR, named as "Genomics for Understanding Rare Diseases India Alliance Network (GUaRDIAN)," for the purpose to bring together and understand novel genetic variations to achieve translational applications by both clinicians and basic science researchers. GUaRDIAN, the pioneer and one of the largest networks of clinicians and researchers in India have been working on rare genetic diseases. The CSIR- IGIB offers a research oriented, well-structured and carefully supervised training programme in rare diseases and related fields.

Indian Collaborative Research Network on Wilson's Disease (ICROWD)

ICROWD is also another programme supported by CSIR at IGIB for Wilson's diseases (WD). WD, a classical monogenic disorder, is the commonest cause of paediatric chronic liver disease in Indian subcontinent and also, one of the few treatable causes of liver disease across all populations. We have already established a pilot network of over 40 clinicians and researchers from over 9 medical and research centres across the country working in the area of WD. The ICROWD has four major components encompassing the clinical areas of WD, the molecular genetic basis of WD, disease modelling and correction of gene defects. For each of the four areas, we have a consortium approach to deliver better diagnosis and personalized, precision medicine in WD clinical settings in India. [5]

Nongovernmental organization initiative

Organization for Rare Diseases India (ORDI; www.ordindia.org) is a voluntary organization which was established to deal with the rare disease conditions in the Indian population. The ORDI team members belong to different disciplines and they need not have a science background. ORDI deals with the matters related to the rare disease such as unique challenges in dealing with rare diseases. [6] The Indian organization for rare diseases was conceived in 2005 and is incorporated as a not-for-profit organization in India as well as in the USA. It is the umbrella organization and represents interests of all rare diseases, individual patients, patient support groups, health policy advocates and health care provider for rare diseases.

Judiciary initiative

In November 2016, the Delhi High Court had ordered the government to finalize a policy on rare diseases and consequently a draft policy was submitted by the Union Ministry of Health to the Delhi High Court on May 25. The Delhi High Court then directed the Centre to implement a National Policy for treatment of Rare Diseases without delay. [7]

Academic institutes

There are many ongoing research projects on various aspects of rare diseases undertaken by reputed institutes such as AIIMS, PGIMER Chandigarh, Christian Medical College, Vellore, and SGPGI Lucknow. It is expected that the outcome of these projects would contribute significantly to solving the existing problems in dealing with rare diseases such as diagnosis,

treatment protocols, causes and genetic basis of the diseases.

Rare Disease Day® is observed worldwide, typically on or near the last day of February each year, to create awareness among policymakers and the public about rare diseases and their impact on patients' lives. [8,9] Each year, NCATS and the NIH Clinical Centre (CC) sponsor Rare Disease Day at NIH as part of this global observance. The global theme for 2019 was "bridging health and social care."

Recently, the Government of India has informed the Hounarable Madras High Court during the hearing of a Public Litigation Petition (PIL) filed by the Lysosomal Storage Disorders (LSD) Support Society of India, New Delhi, that the Government has published a draft policy on rare diseases, seeking public opinion on it. It will be finalized only after considering the views of all stake holders. It is stated that the draft policy envisages a provision of Rs. 150000, for meeting medical expenses, to those suffering from LSD. The draft policy categorises rare diseases amenable to one-time curative treatment such as Haemopoietic stem cell transplantation and those that require organ transplantation into one group. Patients suffering from these diseases are eligible for the relief under the umbrella scheme of Rastriya Arokya Nidhi from Government of India (The Hindu, dated 11.02.2020).

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