CURRENT SCIENCE

Volume 111 Number 1 10 July 2016

GUEST EDITORIAL

Rare diseases need our attention

A large number of diseases have been grouped together as 'rare diseases', because we do not know much about them. There is no consensus on the definition of a rare disease. This is because, obtaining reliable statistical estimates of the frequency of occurrence of a rare event, such as prevalence of a rare disease, requires an inordinately large sample size, collection of which costs prohibitively large amount of money. Recognizing this limitation and the somewhat arbitrary nature of definition of a rare disease, we can use the definition adopted by the World Health Organization: A *rare* disease is a disease whose prevalence in a given country or a region is lower than 1 in 10,000 persons.

It is estimated that, worldwide, there may be roughly 7000 rare diseases, though the basis of this estimate is unclear. In India about 400 rare diseases have been documented. Given the difficulties associated with the diagnosis of a rare disease, the number appears to be a gross underestimate. In the UK, it has been estimated that 1 in every 17–20 people suffers from a rare disease during her/his lifetime (http://www.raredisease.org.uk/about-rare-diseases.htm). If this number applies also to India, then the number of persons suffering from a rare disease exceeds 60 million, substantially larger than the number of cancer patients. Importantly, children are the major sufferers from rare diseases because about 50% of new cases of rare diseases in any country are detected in children below 5 years of age, making it a matter of serious concern to the society.

Clinicians are often unaware of the clinical presentation of most rare diseases, and are unable to provide a correct diagnosis. Therefore, very often a child suffering from a rare disease remains undiagnosed and irrelevant therapies and procedures are tried out on the child, causing more physical and mental harm – and also financial strain. More than 80% of the rare diseases have a genetic basis. This could vary from monogenic with simple Mendelian inheritance, to the involvement of multiple genes with complex inheritance. The problem of diagnosis is compounded by the fact that there could be extensive diversity of mutations in the same gene even for the same disease. Moreover, there is no therapy available for a majority of these diseases, leading to substantial morbidity and mortality. Some rare diseases are also caused by pathogens. Though a substantial number of people may get infected with these organisms, only a handful display disease symptoms and are very difficult to diagnose and treat.

'Rareness' of a disease is a dynamic concept. Infectious diseases that were common in the past may be rare, or even eradicated today. Conversely, diseases not known to occur in India in the past began to be recorded once clinicians became aware of their special diagnostic features. For example, cystic fibrosis was thought to be very rare in India, but genetic analysis has now shown that the disease is prevalent but was earlier undiagnosed. It is generally believed that reported frequency of a majority of rare diseases will go up once diagnostic methods are available and accessible to the population. For a few rare diseases drugs that could slow down the deterioration are available in the international market. However, the costs are prohibitive. In this context, it is heartening that in 2010 the UP Govt sanctioned generous funding to cover the cost of treatment of some haemoglobinopathies. This should be replicated throughout the country and for all diseases where treatments are available. Unfortunately, not a single drug for a rare disease has been developed in this country and the effort in this direction is negligible at present.

Even when mutations resulting in disease phenotype are known, and therapeutic interventions are possible, there is lack of interest among companies in developing diagnostic methods and therapies due to low patient numbers. This lack of interest hampers emergence of newer methods and technologies that could benefit the patients. Moreover, stringent and inflexible regulatory systems do not allow rapid transfer of treatment from lab to the patients. As most of these diseases are degenerative, the condition of patients become worse every passing day if they do not get proper treatment. The rarer the disease, the more serious are these problems. Since the causal factors vary from one disease to another, specific measures are needed for management of each of these diseases.

As a scientific community we need to develop a strategy and come out with a plan to tackle the enormous burden of rare diseases and associated issues of extreme and progressive disability. For this, there has to be a collabo-

rative effort among clinicians, researchers, Government officials, pharma industry, NGOs, patients and students from across the country in a mission mode. We should plan to have an impact within a decade on the following specific issues.

- Mapping and identification of patients with rare diseases and creation of a rare disease registry in the country. This will be helpful in formulating a policy on rare diseases.
- One of the major problems in rare diseases is the lack of awareness not only among common people, but also among clinicians and researchers. A concerted effort should be made to increase awareness.
- We need to set up new centres and strengthen the already existing ones on molecular diagnosis of rare diseases taking advantage of new low-cost technologies that are becoming available.
- A number of Centres of Excellence should be set up as referral and research centers for patient management and for developing therapeutics and diagnostics.
- Alternate forms of therapy, such as Ayurveda should be explored to investigate their potential role in preventing progression and enhancing quality of life of patients.
- In order to enhance mobility of patients with rare diseases, we need to provide adequate assistive devices. This can be achieved through better designing using smart, light weight materials.
- There should be a concerted effort to develop therapies for these diseases and make these accessible and available to all patients. For this we need to enhance our capabilities in technology platforms, such as animal model systems, gene therapy vectors and stem cells in addition to enhancing our abilities to identify therapies based on small molecules.
- A rare/orphan disease policy is required to implement most of the goals outlined here. Currently there is none in India, though 23 countries such as USA, UK, Taiwan, Ukraine and many European countries have already formulated specific policies. However, there has been an attempt to formulate an orphan/rare disease policy for the state of Karnataka. In addition to an enabling policy, the Government needs to allocate resources specifically earmarked for rare diseases.
- Patient advocacy groups should be part of development and implementation of the policy and their suggestions should be sought at every stage.

V. M. Katoch[1]
P. P. Majumder[2]
A. Bhattacharya[3,*]

[1]NASI-ICMR Chair on Public Health Research at RUHS, Jaipur, India
[2]National Institute of Biomedical Genomics, Kalyani 741 251, India
[3]School of Life Sciences, Jawaharlal Nehru University, New Delhi 110 067, India
*e-mail: alok.bhattacharya@gmail.com