A CALL FOR

Millions of children in India suffer from rare diseases that elude diagnosis and treatment

By **Ritu Bhatia** in New Delhi

IF YOU HAVE seen Amitabh Bachhan in the recent Bollywood film *Paa*, you may know that the disease he suffered from, progeria, is a genetic disorder that causes children to age rapidly. What you may not know, however, is that progeria is just one of the thousands of rare diseases affecting millions across the globe. Defined as disorders with an incidence of less than one in 2,000 persons, today there are over 8,000 rare diseases in the world. These have tongue-twisting names like Pompe, Krabbe and Gaucher's.

According to Dr I.C. Verma, chairman, department of genetic medicine, Sir Ganga Ram Hospital, about 35 million people suffer from rare diseases in India. The absence of any formal data collection on such diseases, however, makes it difficult to reach a definitive conclusion about the situation. The lack of an existent system to tackle these disorders makes the situation worse. "Many rare diseases are extremely disabling, life-threatening and challenging. Unfortunately it takes several years for the right diagnosis to be made because minimal research has been conducted in this field. Even when treatment is available, cost constraints may deter patients," says Verma.

The absence of awareness, sound medical guidance and reliable diagnostic tests for this group of diseases are the cause of extreme frustration for parents whose children suffer from illnesses that defeat diagnosis. "It took us five years to confirm that our daughter was suffering from a disease called MPS 1. We had to send the blood sample to Taiwan, for which we had to obtain permission from the health ministry and complete several other formalities," says 41-year-old Deepak Kumar.

Experts here are focused on a group of rare diseases called Lysosomal Storage Disorders (LSDs). This is a collection of 45 rare inherited metabolic disorders, caused by the dysfunction of cells called lysosomes in our bodies, usually as a consequence of deficiency of a single enzyme required for the metabolism of lipids, glycoproteins or mucopolysaccharides. The most common and treatable LSDs are called Pompe, Fabry, Gaucher's, MPS 1, 2 and 7. Like other genetic diseases, individuals inherit LSDs from their parents. All of us carry one or two faulty genes but when both parents are carriers of a faulty gene the chances of getting affected by LSD go up. For instance, Gaucher's disease occurs when a child inherits a damaged gene from each parent whereas Fabry disease is caused when the mother is a carrier of the faulty gene. Although each disorder results from different gene mutations that cause a deficiency in enzyme activity, a common biochemical characteristic unites them.

Symptoms of LSDs can be mild or severe, depending on the particular disorder and other variables like the age of onset. They include developmental delay, movement disorders, seizures, dementia, deafness and/or blindness. Some cause enlarged livers and spleens, pulmonary and cardiac problems, and bones that grow abnormally. Symptoms usually start appearing when a child is between six months and two years old. Even a child who is born normal can develop the symptoms with time. Rare diseases are also called progressive diseases because as the patient ages, the disorder increases in intensity, restricting movement, stunting growth and reducing life expectancy. "Our daughter was born normal but she missed important milestones so we took her to Dr Verma. Even then it took another five years to get the correct diagnosis," says Deepak.

IT REALLY IS a Catch-22 situation: Since the symptoms of LSDs develop slowly, this delays diagnosis, and once the disease has progressed to a certain point, treatment can't reverse it. When motor delays accompany symptoms of LSDs, the prognosis is worse. Diagnostic tests are available only at a few places in India. Apart from this, low awareness among doctors about these diseases and their symptoms often leads to misdiagnosis and wrong treatment. "While more people are approaching us to avail of diagnostic facilities, awareness is still low. Such disorders are regarded as mental retardation even though all of them do not impact the mind," says Dr Ratna Puri, consultant, department of genetics, Sir Ganga Ram Hospital. Misdiagnosis also occurs since many doctors typically conclude that leukaemia or malaria may be responsible for an enlarged spleen and prescribe a treatment regimen for this.

B.N. Saha had no idea that his son suffered from MLS 2, a disorder which delays physical and mental development. It was only six months after his son's birth that Saha noticed the child had stiff knees. It took another two years for doctors to determine the cause. "First we visited orthopaedicians and paediatricians who were unable to pinpoint the reason for the problem. Even after the genetic tests were done, experts confused the disorder with another rare disease. Later on, the samples were sent to a lab in France which settled all the doubts," Saha recalls.

EXPERTS FEEL that one way of preventing this situation from worsening is for the government to make diagnostic tests on newborns for Down's syndrome, hypothyroidism and LSDs mandatory. Pre-birth genetic counselling and DNA analysis test at the time of birth is advised. While predictive or preventive testing is possible, this is generally done only if there is history of a rare disease in a family. A pregnant woman with a family history is advised to get a prenatal test called Chorionic Villus Biopsy done, but this may not always be feasible. "There are thousands of rare diseases which require different diagnostic facilities. It's not possible to test all pregnant women for rare diseases. If the first child or a relative suffers from a rare disease, we carry out specific tests and the couple can then decide to abort the foetus," says Dr Puri.

Even if tests are done, the possibility of error can never be eliminated. The lacunae in diagnostic facilities can be judged from the fact that Saha's second child also suffers from MLS 2 despite the fact that the tests done after 11 weeks of pregnancy were negative. "There's a 25 per cent chance of a second child suffering from a rare disease if the first child already has it. All the genetic tests done before the birth of my daughter predicted that she would be free of any disorder, but now both our children are dependent on us," Saha says.

With inputs from Harsha Chawla and Manu Moudgil

FACTS ABOUT RARE DISEASES

1 Rare diseases are usually detected after six months of a child's birth. Parents should look out for facial abnormalities, stiffness in limbs, slow development and inability to reach key milestones in the process of growth.

2 Get the tests done at a reliable centre since it's very difficult to diagnose rare diseases and most doctors don't know about them.

3 Rare diseases are often treated as a curse and parents are encouraged to have a second child. But in absence of any counselling and tests, there is high risk of a second child being born with the same disease.

4 Consanguinity or marrying within your extended family causes inbreeding which passes abnormal genes down to the child and causes rare diseases.

5 Rare diseases are often dubbed as mental retardation which is wrong. Not all rare diseases affect the brain.

6 There is no effective cure due to lack of research work in this field. However, medicines, which need to be taken lifelong, help deal with certain diseases.

PROMISING TREATMENTS

WITH successful mapping of human genetic makeup, experts are optimistic that gene therapy holds the key to perfect treatment of rare diseases. By reading the genetic map of a person, scientists will be able to pinpoint where the exact fault lies. This will favour specific drug design and hence better results. "Though it's still too early to say what lies ahead, the developments seem promising," says Dr Ratna Puri, consultant, department of genetics, Sir Ganga Ram Hospital.

A new treatment modality called substrate reduction is also showing positive results. For instance, in the case of Gaucher disease substrate reduction therapy, medicines affect the production of fatty molecules so that the deposits are less and hence lesser enzymes are required to prevent accumulation. *By Manu Moudgil*