Diseases and Diagnostics

The burden of being rare

LVPEI opens a new clinic for rare eye disorders to prevent loss of sight in children

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Rare diseases are less frequently diagnosed, which is the reason why most of these rare genetic conditions remain largely unknown to the general medical fraternity.

Rare eye diseases (REDs) are even less common. But many rare eye conditions are intrinsically associated with certain systemic diseases, and a large number of systemic maladies are manifested through rare eye conditions.

“50% of rare eye conditions have a systemic association and vice versa,” says Dr Muralidhar Ramappa, Consultant Ophthalmologist, Head of Rare Eye Diseases, The Cornea Institute, L V Prasad Eye Institute, Hyderabad.

Ophthalmologists, as one of the first contacts, are usually the first to detect many such rare conditions. “Eye specialists are able to see the interior of a person’s eye, including the retina. They can see what is going on and diagnose some of the rare disease signs very early. This is a rare privilege no other clinician enjoys,” he adds.

REDs are, in most cases, serious, chronic, debilitating and life-threatening illnesses, often requiring long-term and specialised treatments or management. Besides, they often result in some form of handicap, sometimes extremely severe.

More than 50% of the rare diseases occur in children and REDs represent some of the leading causes of childhood blindness.

Most of the RED phenotypes have an early onset. This makes it often preclude a thorough clinical diagnosis at the early stages of the disease.

Arriving at an accurate diagnosis is a big challenge due to the extreme clinical and genetic heterogeneity of rare diseases.

When a patient comes into the clinic with a rare eye condition, it often creates a diagnostic confusion. Without arriving at a correct diagnosis, the physician and the patient’s family will never know what the child is going through or the long-term outcome of the condition, including whether the underlying condition has a sight-threatening or life-threatening association.

Eyeing early care

The Center of Excellence for Rare Eye Diseases (CERED), which has been launched recently at L V Prasad Eye Institute, Hyderabad is a first-of-its-kind centre focused exclusively on advancing eye care and treatment of patients who are diagnosed with rare eye diseases or eye condition related to rare systemic diseases.

“The idea of CERED is to provide comprehensive medical care to the patients under one roof with all inter-departmental, intradepartmental expertise,” explains Dr Muralidhar.

Apart from ophthalmologists, the paediatrician, the metabolic specialist and the genetic specialist will all be together in one room.

Instead of running from pillar to post, the family of the patient can have an accurate diagnosis and a clear roadmap for future directions at a single point.

Early diagnosis is absolutely key to the outcome of such conditions. Blindness resulting from conditions like lysosomal storage disorder can be effectively prevented if diagnosed early and treated with enzyme replacement therapy.

Many of REDs can be accurately picked up during prenatal screening itself. Since the eyes develop in the early stages of the foetus, a careful sonologist can easily detect over 90% of the eye conditions as early as the 12th week of pregnancy. Unfortunately, even conditions like anophthalmia or the total absence of eyeballs is often missed out in the routine antenatal screenings, especially in the non-urban settings in India, Dr Muralidhar points out.

RED Registry in the works

REDs affect more than one in 10,000 people in a given country, according to WHO. There are around 7,000 rare diseases globally. Indian Council of Medical Research (ICMR) has so far documented nearly 450 rare eye diseases.

These figures could be a gross underestimate. The prevalence rate could well be more because 80% rare diseases have genetic causes. Practices like consanguineous marriages, which are largely unknown to western societies, are quite common in the country.

Dr Muralidhar and the CERED team, which is currently working on an India-specific Rare Eye Diseases Registry, has drawn up a list of at least 800 rare disorders which have some ophthalmic association.

Despite the fact that rare diseases are low in prevalence and individually rare, collectively they affect a considerable proportion of the population in any country.

According to generally accepted international research, it impacts between 6% and 8% people.

A lot of rare eye disorders are peculiar to Indian communities.

Some of them are extremely rare or even unheard of in the Western societies. For

example, primary congenital glaucoma is found very, very rarely — perhaps once in 20,000 or rarer in the Western population.

However, in India, the condition is pretty common and occurs as frequently as once in 2,500 live births. Similarly, the country reports a huge number of xeroderma pigmentosum, basically a severe skin condition involving the eyes and other vital organs, which is more or less unseen in western data.

Retinitis pigmentosa, keratoconus and various lysosomal disorders are among the other rare disorders which are found in very high frequencies in India.

Salvaging sight; saving children

Among the growing list of rare diseases, quite a few are life-limiting as well. Estimates show that rare diseases are responsible for 35% of deaths before the age of 1 year, 10% between the ages of 1 and 5 years and 12% between 5 and 15 years. The impact on families is often catastrophic in terms of emotional as well as a financial drain, as the cost of treatment is prohibitively high.

“One of the most painful things for parents is losing their own child in front of their eyes. This is something that CERED wants to prevent,” remarks Dr Muralidhar.

In areas where very early or consanguine marriage rates are high, the prevalence of REDs is also higher. Such rare inherited conditions that run through families can affect more than one child by the same parents. One of the stated objectives of CERED is that no family should have their second child with the rare eye condition. “We can at least put them into genetic counselling to convey the amount of risk that their second child may also have the same problem,” explains Dr Muralidhar.

According to him, as many as 60% of REDs can be cured or managed effectively if accurate diagnosis is made within time. The advent of genomics and other advanced tools and technologies increases the possibilities even more.

A recognised centre for corneal transplantation in children, LVPEI currently offers cutting edge surgical techniques such as selective lamellar corneal grafting, as well as stem cell transplantation trials to treat ocular surface dysfunctions, corneal opacities etc.

The centre also conducts research in selective endothelial removal (SER), kerato-limbal-allografts (KLAL), rotational-auto-keratoplasties and gene editing in corneal dystrophies using lentivirus vector technology platforms.

Researchers at CERED are also exploring an innovative gene-editing tool using nanoparticles delivered to the eye in the form of eye drops.

Further, they are planning to test the pathogenic potential of novel risk alleles and their combinations across RED phenotypes to ascertain their role as genetic modifiers.

CERED is collaborating with some of the world’s best centres in this field. So even if a child comes with a condition not listed in the 7,000-odd rare diseases identified so

far, the centre would strive to provide a diagnosis within one year, in line with its motto: ‘Let no child go blind due to a rare eye disease’.