

ICMR to conduct first nation-wide newborn screening for genetic disorders

Rita Dutta - Mumbai

Parents of seven-year old mentally challenged Kiran (name changed) wonder why their son was not detected with phenylketonuria (PKU), a rare genetic disorder, when he was a newborn. "If Kiran was screened for certain genetic disorders, while he was in the NICU for several days just after his birth, my son would be leading a normal life today," laments Kiran's distraught father. Studies reveal that about 1/3rd of paediatric mental retardation cases stem from the inability to detect a metabolic disorder in early childhood.

Taking cognisance of the grave situation, the government will introduce the first nation-wide mass screening programme in newborns to detect "Inborn Errors of Metabolism (IEM)," a group of rare but potentially lethal genetic disorders. IEM, in which the body's metabolism fails, is usually caused by defects in the enzymes involved in the biochemical pathways.

Project to screen one lakh newborns

The pilot study to be conducted by the Indian Council for Medical Research (ICMR) will be executed by a task force comprising clinicians, paediatricians, geneticists and lab scientists. According to a research officer of ICMR, associated with the project, "The programme is in the preliminary stage and discussions are still on about the various modalities of the project."

The pilot study would probably cover over 1,00,000 newborns from Mumbai, New Delhi, Cochin, Hyderabad. The project costing over Rs one crore and is likely to be completed over two years, added the official.

Explains Dr I C Verma, head, department of genetic medicine, Sir Gangaram Hospital, New Delhi and a member of the task force, "The study is aimed at an early detection and intervention of some genetic disorders along with studying the prevalence of these genetic disorders in different parts of the country. Though five to six private labs are screening newborns for genetic disorders at a cost, the ICMR programme is the first nation-wide screening, which is free."

Of the over thousand existing metabolic disorders, the task force will shortlist around three to four disorders for screening. "Though no consensus has been arrived at on the specific disorders to be screened, the probable ones during the first phase of the study are Congenital Hypothyroidism and Congenital Adrenal Hyperplasia, which are common and for which intervention and management are possible," the ICMR official added.

Says clinician and member of the task force Dr Sharad Gogate, "The programme will only detect disorders which are treatable. It is futile to conduct screening programmes for such disorders, if we cannot correct the underlying physiology." If the pilot project is successful, then a proposal of an expanded mandatory programme covering the entire country and screening more disorders will be mooted to the planning commission. "From a research project, it would thus evolve to be a service project, and can then be included in the maternal child health programme so as to encompass the entire country," adds Dr Gogate.




Logistics

Hospitals, both private and public, having a good number of newborn deliveries, infrastructure for genetic counselling and diagnostic labs would be selected for the project. For hospitals having sufficient newborn delivery but lacking in infrastructure and manpower, resources of other centres would be pooled, adds Dr Gogate.

The screening would involve biochemical assays and not DNA-based analysis. For the test, a drop of blood from the heel of a newborn would be collected and allowed to dry on a filter paper before sending it for screening. The test will be conducted after three days of the birth of the newborn, when the metabolic activity of a newborn takes over the body functions.

The task force is still considering whether it would restrict the programme to screening and not include confirmatory tests like plasma amino acid analysis, urine amino acid analysis, urine organic acid, conducted in metabolic disorder labs. It is sometimes difficult to diagnose IEM in neonates as they tend to get misdiagnosed with sepsis or other disorders. Sepsis often accompanies IEM and may confound diagnosis further, an expert informs.

The various challenges in implementing this project are dealing with funds crunch, locating hospitals which retain newborns for more than three days and convincing the hospitals to participate in the project, which is on no-profit-basis. Though the task force was constituted in 2002, the project faced a few hiccups because of paucity of funds. The task force is soliciting to buy diagnostic kits at a reduced price to tide over the funds crunch.

		
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member of the ICMR task force	NICUs may have IEM Dr Anil Jalan, consultant in paediatric metabolic disorders, MGM Hospital, New Bombay	Madon, geneticist, dept of Assisted Reproduction and Genetics, Jaslok Hospital
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First nation-wide programme

IEMs, which are rare individually but collectively common, can appear anytime and form an important cause of morbidity and mortality in infants and children, says Dr Verma, former head of department of genetic medicine at All India Institute of Medical Sciences, New Delhi.

No comprehensive nation-wide study on prevalence of IEM has been conducted in India so far, except some hospital and state studies. Is the situation that acute? Statistics definitely say so. Of 25 million babies born in India every year, it is estimated that 1 in every 2000 newborns suffers from metabolic disorders. The incidence varies from community to ethnicity to religion to location. For instance, while hypothyroidism is prevalent in sub-Himalayan areas, sickle cell disease is common in the tribal populations of Maharashtra, Gujarat, Orissa, Madhya Pradesh, Kerala and Tamil Nadu, including the non-tribal population from Chattisgarh State, state various studies.

According to Dr Anil Jalan, consultant clinical and biochemical geneticist and a specialist in paediatric metabolic disorders, MGM Hospital, New Bombay and a member of the task force, "Of thousands of children in India who die of Sudden Infant Death Syndrome, the death of an infant below one year, around five to ten per cent have IEMs. Around 15-20 per cent of new born babies admitted to NICUs may have IEM." He has observed that around 17 per cent of babies in NICUs have IEM like Galactosemia, Biotinidase deficiency, MSUD, Propionic acidemia, Methyl Malonic acidemia, OTC deficiency, which are much more common in India than the western world.

Screening for metabolic disorders in newborns, pioneered by Prof Robert Guthrie in 1960, has now become mandatory in the US, Europe and Southeast Asian countries like Australia, China, Korea, Thailand, Phillipines, Singapore and Bangladesh.

The disorders mostly screened are phenylketonuria and congenital hypothyroidism, galactosemia, sickle cell disease, congenital adrenal hyperplasia, maple syrup urine disease (MSUD), homocystinuria, and biotinidase deficiency.

Criticism

Welcoming the ICMR programme, Dr Prochi F Madon, consultant geneticist, department of Assisted Reproduction and Genetics, Jaslok Hospital, says, "Some of these rare disorders are

preventable and treatable, and if detected in time, can help reduce morbidity and mortality. Detection of genetic disorders in newborns, aid in saving their lives, mainly through proper dietary management.”

The screening programme is the first step towards addressing a gamut of issues plaguing the diagnosis and treatment of genetic diseases. “To make the diagnosis and treatment more affordable, the government needs to reduce custom duty on kits, medial equipment and dietary supplements, which is a whopping 30 to 35 per cent,” says Dr Jalan.

Dietary therapy is the mainstay of treatment in phenylketonuria if detected in the newborn, and can help to prevent mental retardation. “Homocystinuria, galactosemia, glycogen storage diseases, certain varieties of MSUD, urea cycle disorders and organic acidemias also require dietary modification,” explains Dr Madon.

The cost of a can of dietary supplement is Rs 2500 and above. With three to four cans required for a month, the cost of dietary supplement is a staggering Rs three lakh and above for a year, making it unaffordable. “As most parents find it difficult to afford these diets, it is therefore important that these diets be exempted from customs duty,” suggests the ICMR official.

Various Prevalence Studies

1 In 2002, Hyderabad-based Centre for DNA and Fingerprinting Diagnostics (CDFD), aided by Dr Reddy’s Foundation for Human Development had conducted DNA tests on about 5,000 newborns in four government hospitals to detect genetic disorders. Using chromatographic (TLC and HPLC), electrophoretic (cellulose acetate and agarose) and ELISA based assays for screening, the study revealed a high prevalence of congenital hypothyroidism (1 in 1700) followed by congenital Adrenal Hyperplasia (1 in 2575) and Hyperhomocystenemia (1 in 100).

2 According to a screening programme held at AIIMS, the four commonest disorders in northern India were homocystinuria, alcaptonuria, maple syrup urine disease and nonketotic hyperglycinemia.

3 The first newborn screening was carried out in 1980 in Bangalore for aminoacid disorders involving 125 thousand newborns. Screening the high-risk populations, Homocystineimiamia, hyperglycinemia, MSUD, PKU, Hypothyroidism and G6PD deficiency were found to be the common causes of mental retardation.

The answer lies in developing indigenous dietary supplements. Several nutritional research institutes and centres in the country are already on the trail for developing indigenous supplements. “The supplements are effective and cheap, but they have to be tried on clinical trials and marketed at the earliest,” avers Dr Gogate.

Experts point out that policy makers need to tread with caution with MNC’s hardselling diagnostic kits, equipment and diet supplements in the Indian market. “With 25 million babies born per year, India forms one sixth of the market for such products. But where is the infrastructure? We have only a few experts in metabolic medicine to deal with such newborn screening, confirmatory tests and therapy,” says a concerned paediatrician.

Awareness about symptoms of IEM and its initial diagnosis among physicians and paediatricians also needs to be enhanced.