Universal Newborn Screening – Is it Going to be a Reality in India?

Neonatologist's Perspective

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Universal newborn screening is quite well established in most of the developed countries. In India, the exact prevalence of various metabolic disorders is not known due to lack of any large scale multicentric study to screen metabolic disorders and absence of any organized system of universal newborn screening. Like other developing countries, India is facing an increasing challenge of non-communicable diseases, of which many are preventable. Endocrinopathies and other genetic/metabolic diseases constitute an important proportion of such problems. The unique clinical dilemma with these disorders is that either they are asymptomatic or have only non-specific signs and symptoms in the early stages, thereby rendering their early diagnosis almost impossible without a screening program. Some of these disorders like congenital hypothyroidism have a debilitating impact on the developing neonatal brain, if not diagnosed early.

The major hindrances for establishing an effective screening program in India are the costs involved, the non-availability of demographic data about the diseases in question, massive annual birth cohort and the limitations of treatment modalities for some of the diseases. The Wilson criteria [1] mandates such factors and data for the cost effective and efficient running of a screening program, including diseases like congenital hypothyroidism. However, recent developments in the health infrastructure of India and the availability of data on some of these conditions have addressed these problems to a certain extent. For example, in a hospital based survey, 5.75% of all intellectual disability were attributed to metabolic diseases [2]. A previous pilot newborn screening program conducted in Southern India screened 1,25,000 infants and identified homo-cysteinemia, hyperglycinemia, Maple syrup urine disease, phenylketonuria, hypothyroidism and Glucose-6-phosphate dehydrogenase (G6PD) deficiency as the most common metabolic errors [3]. A more recent study documented similar results with particularly high incidence of congenital hypothyroidism (1 in 1700); congenital adrenal hyperplasia, G6PD deficiency and amino-acidopathies were the other common disorders. This study estimated the prevalence of any metabolic disease as 1 in 1000 [4]. More recent preliminary results from Chandigarh [5] and Andhra Pradesh [6] also indicate a high incidence of metabolic diseases in Indian population.

The sample collection and processing have been simplified by the establishment of filter paper sampling method (dried blood) from a heel prick. This allows a convenient way for collection and transport of the sample. The advances in the tandem mass spectroscopy allow the detection of most of the inborn errors of metabolism relatively easily. One major obstacle in our country is the timing of sampling. The general guidelines of obtaining a heel prick sample between day 3 to 7 is very difficult to follow in India due to massive load of deliveries leading to early discharge from the hospital, and a high proportion of home deliveries. To counteract this problem, countries like Malaysia and Cuba have tried screening with cord blood sample for congenital hypothyroidism, but this strategy is not valid for other metabolic diseases like aminoacidopathies. In a Quebec–New England collaborative study of normal newborns, it was shown that the TSH estimation at 24-48 hours of life is comparable with estimation at a later duration [7]. The study in this issue by Gopalakrishnan, *et al*. [8] used the same strategy. The concern of diagnostic cut-off of TSH level is an important point in our set up. Selecting a lower universal cut-off point may increase the sensitivity but will hugely increase the false positive results and recall rates which will overload the facilities. The usage of age appropriate cut-offs is the most logical method in this setting and this was ably demonstrated in the current study. The problem of loss to follow-up and non-availability of the newborn for recall for a confirmatory sample (in case the screening test is abnormal) still exists. In the current study, the authors could not perform the repeat test in 15% of babies. The MCTS (Mother child tracking system), an initiative launched by the Government of India, once fully implemented may play a pivotal role in rectifying this problem.

In the current study, authors tried the feasibility of screening and recall system for newborn screening for congenital hypothyroidism, galactosemia and biotinidase deficiency, in a rural population of UP, India. They used heel prick sample, collected at 24 hours of life in 13426 newborns, constituting 73% of all deliveries. From those with abnormal screening results, 85% could be recalled for the confirmatory test and they identified 11 babies with congenital hypothyroidism. Compared to Western data, this loss to follow-up is significant but previous experience from India [5] documents even a higher loss to follow-up. As the loss to follow-up will reduce the impact of the program to a great extent, this emphasizes the need for a proper tracking schedule. The Goa screening program has shown that an effective follow-up can be ensured even in a public set up [9].

The authors have shown that the neonatal screening program is feasible even at a rural set up and also demonstrated the high incidence of congenital hypothyroidism. The failure to sample about 27% of newborns and the significant loss to follow-up are the matters of concern. This paper further establishes the need of a nationwide screening strategy and strengthening the follow-up care. The establishment of a screening program in a country like India will require huge investment by the government, but as evidenced by the experience in developed countries, this strategy will be cost effective in the long run. Experience from the public (Goa and Chandigarh) and various private sectors in India should provide the platform to the Government for establishment of an effective neonatal screening program.

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Newborn Screening: The Critical Importance

Biochemist's Perspective

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Newborn screening (NBS) is a public health program designed and developed to screen infants shortly after birth. The principle of NBS Program is to detect potentially harmful disorders that are not clinically evident at birth. Newborn screening is a success story in USA [1,2] and European countries [3] despite different approaches to timing of screening, follow-up testing and intervention [4]. In India, the concept of NBS is in the nascent stages, and as of now is more focused on detecting congenital hypothyroidism, congenital adrenal hyperlplasia, galactosemia, Glucose-6-phosphate dehydrogenase deficiency, biotinidase deficiency and cystic fibrosis. Screening for inborn errors of metabolism, including aminoacidopathies, organic acidemias and fatty acid oxidation disorders are yet to pick up as the costs involved are daunting [5]. False positive alarms and recall rates of a NBS program depend on methodology used and quality of diagnostic services. For