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Editorial Commentary

Achieving developmental goals in congenital hypothyroidism – Strategies for a post-screening era

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Congenital hypothyroidism remains the most common preventable cause of neurocognitive disability.[1] Global implementation of neonatal screening programs for congenital hypothyroidism has drastically reduced its burden of development delay; the lack of a unified national congenital hypothyroidism screening program remains a major impediment in preventing the adverse developmental outcome due to this disorder in India.[2,3]

Recognizing the importance of identifying congenital hypothyroidism has resulted in the institutional and regional implementation of neonatal screening programs. These programs have enabled the identification of children with congenital hypothyroidism within the intervention window, highlighting the need of appropriate management to achieve good long-term outcomes. Identifying determinants of neurodevelopmental outcomes in individuals with timely initiation of thyroxine treatment remain the mainstay for improving outcomes in the post-screening era. Initiating treatment in the first month of life at a high dose with rapid normalization of thyroid functions and good adherence to therapy are the key determinants of good long-term development outcomes in congenital hypothyroidism.[2,4,5]

There is a paucity of data regarding the neurodevelopmental outcome of congenital hypothyroidism in Indian children. In this journal issue, Singh *et al.* report their study on the correlates of development (assessed by Bayley Score for Infant Development-III, BSID-III) in 53 children with congenital hypothyroidism at the mean age of 2.5 years. Nearly, all of these were identified on neonatal screening and started on thyroxine treatment within 3 months of life.[6] A key aspect of this study was the close monitoring of thyroid functions in the first year of life (weekly till the normalization of thyroid-stimulating hormone [TSH] and monthly thereafter).

The authors observed normal mean BSID-III scores across all domains. Impaired cognitive and motor development was noted in only one individual treated after 3 months of age. The time taken to normalize the TSH level was the only significant correlate for BSID-III estimated motor score, with no correlation with the time of initiation of therapy, initial TSH level, and thyroxine dose. This suggests that rapidly achieving euthyroid status is the key determinant of neurodevelopment outcomes in individuals treated at an appropriate age (below 30 days) with an adequate dose (above 10 μg/kg/day). The similar impact of low (10–12.5 μg/kg/day) and high (12.5–15 μg/kg/day) initial thyroxine dose has been demonstrated in a multicentric randomized control trial, suggesting that the wide dose range of 10–15 μg/kg/day is effective in preventing adverse neurological outcome in congenital hypothyroidism.[7] A study evaluating intellectual outcomes in children with congenital hypothyroidism suggested that the therapeutic window

for initiation of thyroxine therapy may extend to 30 days, as reflected by the observation that all the subjects with neurodevelopmental delay in the study (6%) were treated after the age.[8] These observations highlight the importance of initiating therapy within 30 days of life at a thyroxine dose above 10 μg/kg/day.

Demonstrating excellent neurodevelopment in children with congenital hypothyroidism identified at the appropriate age and carefully managed with appropriate thyroxine dose makes a strong case for neonatal screening. Given an incidence of congenital hypothyroidism of 1 in 1500 and the likelihood of missed diagnosis within 1 month in 60%, over 20,000 children are expected to suffer from avoidable neurocognitive disability every year in India due to the lack of a national screening program.

A key takeaway from the study is the need for rapid normalization of TSH to improve neurological outcomes in congenital hypothyroidism. This, however, needs to be balanced by avoiding overtreatment, as reflected by lower intelligence quotient (IQ) scores in individuals with persistently high free T4 levels in the first 2 years of life.[9] Studies have shown persistent deficits, especially in the expressive language domain, despite timely identification and appropriate treatment.[4] The superior neurodevelopmental response in the present study may be related to closer monitoring in the first year. Less than seven visits in the first year of life is a risk factor for a worse neurodevelopmental outcome. As suggested in the study, the benefits of weekly monitoring of TSH in the titration phase need further exploration before widespread implementation. The relatively short follow-up duration (2.5 years) is a limitation of the study, as the contribution of treatment-related variables is higher at an older age group (35% for verbal IQ at 2.6 years as compared to 19% at 2 years).[10] This reflects the need for longer follow-up before wider implementation.

The study's finding is a poignant reminder of the devastating effects of missed congenital hypothyroidism. The study reassures the normal developmental outcome with timely diagnosis and provides direction toward appropriate management strategy. While the factors affecting intellectual outcomes in individuals diagnosed with congenital hypothyroidism by neonatal screening need to be determined in larger prospective studies, the importance of screening for neonatal hypothyroidism cannot be emphasized.

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