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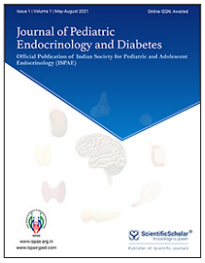

Editorial

Hypothyroxinemia of prematurity – Is it really transient and benign?

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Transient hypothyroxinemia of prematurity (THOP) is a condition, where preterm babies have low free T4 (fT4) levels and a normal TSH after birth.[1] It can affect up to a quarter of babies born preterm below 34 weeks of gestation. Babies with other comorbidities tend to be affected more. Although the fT4 levels normalize after few weeks, it is not clear when this would happen and if there is a risk of long-term neurodevelopmental sequelae. There is no evidence that treatment with thyroxine alters the outcome and, therefore, not generally recommended.[2] Babies with delayed rise of TSH, secondary/tertiary hypothyroidism may also present similarly and have to be differentiated from this condition.

Most preterm babies have normal TSH secretion in response to inadequate circulating thyroid hormone levels. This means that primary hypothyroidism in a preterm baby can be detected by routine testing of TSH values. However, some preterm babies have inadequate TSH secretion in response to decreasing fT4 levels. There are many factors contributing to this.[3] Immaturity of the hypothalamic–pituitary–thyroid axis is often implicated particularly in extremely low birth weight babies. Acute illnesses such as respiratory distress syndrome, sepsis, anemia, and birth asphyxia can also contribute to this, and sometimes, this is part of "euthyroid sick status" or "non-thyroidal illness." Thyroid-binding globulin deficiency, iodine deficiency, and drugs such as steroids and dopamine can also impair circulating thyroid hormone levels. Hypothalamic or pituitary causes (secondary or tertiary hypothyroidism) can also cause low fT4 levels with normal TSH which can be transient or permanent.

There is no clear consensus regarding the timing of testing in babies with THOP. While the American Academy of Pediatrics 2006 guidelines suggest serial measurements of T4 until they become normal, the European consensus guidelines recommend repeating thyroid test at 10–14 days.[4] "Newborn Screening Guidelines for Congenital Hypothyroidism in India" published by the Indian Society for Pediatric and Adolescent Endocrinology (ISPAE) recommends routine screening for all preterm infants at 48–72 h of age, followed by a second screening test at 2–4 week of age for high-risk babies.[5]

In this issue, Gaonkar *et al.* have published an article titled "A study of the normalization of hypothyroxinemia in neonates below 34 weeks of gestation," where the authors have studied the time of normalization of THOP in 69 babies born below 34 weeks gestation.[6] The study is a retrospective analysis that also looks at neurological outcome at 18 months when compared to babies with no THOP. Only two babies have required treatment with levothyroxine in this study that too for a very brief period. There were no congenital hypothyroidism in this cohort and there is no mention of babies with delayed rise of TSH. The time for normalization was

14 days in most babies and 28 days in high-risk babies.

The results of this study have to be interpreted with caution. The cutoff for fT4 used in this study (<15.5 pmol/L for <14 days and <12 pmol/L for >14 days) is little different to other studies and those that are recommended by ISPAE's "clinical practice guidelines" published in 2018.[7] The cutoff value for fT4 recommended by ISPAE guidelines is below 1.1 ng/dL (14.2 pmol/L) irrespective of TSH value. There are no differences in cutoff value according to age of the baby in the ISPAE guidelines.

The authors have reported statistically significant difference in the prevalence of developmental delay at 18 months in babies with THOP, although the different domains of development have not been studied. The contribution of various neonatal morbidities to this delay in development is not very clear. It is quite possible that in high-risk babies, similar clinical variables might cause low fT4 values as well as developmental delay. Further, long-term studies involving larger number of patients are required to address this issue. This is important as questions remain whether there is a sub-group of babies with THOP who may benefit from levothyroxine supplementation. It is worth remembering that unnecessary or inappropriate thyroxine therapy may lead to adverse consequences including poor neurocognitive outcome.

In a resource limited setting like India, it is difficult to do repeated thyroid testing in babies and the priority remains to implement universal newborn screening so as not to miss congenital hypothyroidism.[8] Decisions regarding levothyroxine treatment should be individualized and taken after considering all the factors.[9]

REFERENCES

1. De Escobar GM. The hypothyroxinemia of prematurity. J Clin Endocrinol Metab 1998;83:713-5.
2. Hollanders JJ, Israëls J, van der Pal SM, Verkerk PH, Rotteveel J, Finken MJ, *et al*. No association between transient hypothyroxinemia of prematurity and neurodevelopmental outcome in young adulthood. J Clin Endocrinol Metab 2015;100:4648-53.
3. Yilmaz A, Ozer Y, Kaya N, Turan H, Acar HC, Ercan O, *et al*. The factors associated with transient hypothyroxinemia of prematurity. BMC Pediatr 2021;21:344.
4. Szinnai G, Murray P, Bartés B, Luton D, Salerno M, de Sanctis L, *et al*. Congenital hypothyroidism: A 2020-2021 consensus guidelines update-an ENDO-European reference network initiative endorsed by the European society for pediatric endocrinology and the European society for endocrinology. Thyroid 2021;31:387-419.
5. Desai MP, Sharma R, Riaz I, Sudhanshu S, Parikh R, Bhatia V. Newborn screening guidelines for congenital hypothyroidism in India: Recommendations of the Indian Society for Pediatric and Adolescent Endocrinology (ISPAE)-part I: Screening and confirmation of diagnosis. Indian J Pediatr 2018;85: 440-7.
6. Gaonkar S, Shenoi A, Sathyanarayana SO, Namachivayam AK, Raja DM, Rao N. A study on normalization of hypothyroxinemia in neonates below 34 weeks of gestation. J Pediatr Endocrinol Diabetes 2022;2:56-62.
7. Kusuma SB. Newborn Screening for Congenital Hypothyroidism (NBS-CH) Clinical Practice Guideline Algorithm Based on ISPAE, CH-2018 Guidelines; 2021. Available from: https://www.ispae.org.in/wp-content/uploads/2021/05/NBS-for-CH-Algorythm.pdf [Last accessed on 2022 Oct 05].
8. Bhatia V. Hypothyroxinemia in preterm neonates: Not always hypothyroidism. Indian J Pediatr 2019;86:671-2.
9. Yoon SA, Chang YS, Yang M, Ahn SY, Sung SI, Cho HS, *et al*. Effect of levothyroxine supplementation in extremely low birth weight infants with transient hypothyroxinemia of prematurity. Sci Rep 2022;12:9717.

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