Editorial

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Reconsidering the timing of levothyroxine discontinuation in children with congenital hypothyroidism: insights from a Korean Cohort Study – commentary on "Predicting variables associated with diagnostic reevaluation of transient congenital hypothyroidism"

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In this issue of *Annals of Pediatric Endocrinology & Metabolism*, Gwag et al. [1] present a well-designed retrospective cohort analysis investigating predictors of transient congenital hypothyroidism (TCH) and the feasibility of early discontinuation of levothyroxine (LT4) in affected children. The study analyzed 167 Korean patients diagnosed with congenital hypothyroidism (CH), of whom 57.5% were classified as TCH and 42.5% as permanent CH. The authors found that shorter gestational age and lower LT4 doses at 18 and 24 months were significantly associated with TCH. Through Cox regression and receiver operating characteristic (ROC) analysis, they identified a threshold dose of 3.03 μg/kg/day at 18 months that effectively predicted successful early withdrawal (sensitivity 75.0%, specificity 72.9%).

These findings are particularly timely given the rising global increase in TCH , likely driven by expanded neonatal screening and improved sensitivity in detecting mild or subclinical hypothyroidism. The study contributes valuable evidence in support of individualized treatment timelines and challenges the conventional recommendation to re-evaluate thyroid function only after 3 years of continuous therapy.

A key strength of this study is its use of real-world clinical data from a Korean pediatric population, enhancing regional applicability and generalizability within similar healthcare settings. Furthermore, the statistical methods employed—particularly the use of time-to-event analysis and ROC curves—offer a robust framework for identifying early predictors of TCH. The proposed LT4 dose cutoff provides a practical tool to inform clinical decisions, especially in contexts where few validated early discontinuation criteria currently exist. This is consistent with recent updates to clinical guidelines from the European Society for Paediatric Endocrinology (ESPE) and the American Academy of Pediatrics, both of which now support earlier reassessment in selected cases- such as those with gland-in-situ and low LT4 requirements.

Despite these contributions, the study leaves an important clinical gap unaddressed: the management of children who, after LT4 withdrawal, maintain mildly elevated thyroid-stimulating hormone (TSH) levels between 4.5 and 10 μIU/mL—a biochemical profile consistent with subclinical hypothyroidism (SH). Although these patients do not meet the diagnostic criteria for overt hypothyroidism, the optimal management strategy remains unclear. Current pediatric endocrine guidelines suggest that asymptomatic children with TSH <10 μIU/mL and normal free thyroxine (fT4) levels may be safely monitored without intervention. However, in practice, this subclinical range often presents a diagnostic dilemma, particularly in young children whose neurodevelopment is still ongoing [2,3].

The long-term effects of sustained SH during early childhood are not well defined [4]. Although available evidence indicates that most children with mild TSH elevations spontaneously normalize without adverse cognitive or growth outcomes [5-7], concerns persist. Some adult studies have linked persistent TSH elevation in this range with subtle thyroidal hyperplasia and increased risk of cyst or nodule formation [8,9], though pediatric-specific data

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are limited. Furthermore, the neurodevelopmental vulnerability of infants and toddlers warrants a more cautious approach than might be taken in adolescents or adults. In this context, the absence of follow-up data for children with borderline TSH elevations post-withdrawal limits the generalizability of the study's early discontinuation criteria.

Future research should aim to clarify the clinical trajectory of these subclinical cases. Prospective studies incorporating long-term outcomes such as cognitive development, thyroid morphology, and biochemical normalization rates would provide much-needed guidance for clinicians navigating this gray zone. Importantly, such efforts should consider not only static TSH thresholds but also dynamic trends over time, in conjunction with clinical features such as goiter presence, thyroid antibody status, and growth metrics.

In summary, Gwag et al. provide a thoughtful, data-driven framework for optimizing LT4 treatment duration in children with CH. Their findings underscore the importance of risk-based, individualized management strategies that balance of both overtreatment and undertreatment. Nevertheless, as early discontinuation becomes more acceptable in selected patients, attention must also be directed toward those whose thyroid function remains borderline—an underexplored yet clinically consequential subgroup.

As neonatal screening and diagnostic tools continue to evolve, our therapeutic algorithms must evolve as well. This study marks a welcome step toward more personalized care in pediatric endocrinology and highlights the ongoing need for nuanced, evidence-based frameworks in managing CH.

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